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An independent academic psychologist, based in England, who has written extensively on different areas of psychology with an emphasis on the critical stance towards traditional ideas.

A complete listing of his writings at http://psychologywritings.synthasite.com/ and http://kmbpsychology.jottit.com.

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1. TRYING TO UNDERSTAND THE BIOLOGICAL BASIS OF SEXUAL DIFFERENTIATION

1.1. BIOLOGICAL SEX DIFFERENCES

Arnold et al (2016) summed up their area of research: "The study of biological sex differences attempts to identify, categorise and understand the inherent factors that make the two sexes different from each other. These include factors that make every female different from every male (and vice versa). In addition, some factors cause the two sexes to be different, on average, even though some individuals of each sex are similar to individuals of the other sex. Our general goal is to distinguish and understand the separate components causing sex differences" (p1).

1.1.1. Sex Chromosomes

In mammals, it is assumed that the presence of the Y chromosome in males is key in sexual differentiation (ie: males have XY chromosomes and females XX). But recent work, particularly with mice, has shown that the X chromosome also plays a role (Arnold et al 2016) [1].

Transgenic mice can be produced with testes in both sexes (known as XXM and XYM) or ovaries (known as XXF and XYF) to compare chromosome differences independently of gonad (ie: testes or ovary) (known as the Four Core Genotypes (FCG) model), while the XY* model (ie: XO, XX, XY, XXY versions) can test the effect of the Y chromosome (Arnold et al 2016).

[1] The X chromosome genes can be affected by parent-of-origin effect (ie: the same gene behaves differently depending on its origin from the mother or father) (Arnold et al 2016).

These models show that "mice with one X chromosome can be strikingly different from those with two X chromosomes, when the differences are not attributable to confounding group differences in gonadal hormones. The number of X chromosomes affects adiposity and metabolic disease, cardiovascular ischaemia/reperfusion injury [2] and behaviour" (Arnold et al 2016 p1).

Leopard geckos (like most lizards), for instance, do not have sex chromosomes, as in humans or birds [3], and biological sex is determined by temperature of egg incubation (Wade 2016).

It is assumed that hormones are key, then, in sexual differentiation, but research with lizards and birds has found that the effects of testosterone, for example, not only vary between the sexes, but in the same individual across seasons and between tissues (Wade 2016). Wade (2016) concluded that other neurochemicals must be involved (eg: brain-derived neurotrophic factor, BDNF).

Also "perfectly good male or female brains and bodies can develop from an identical genome, based on differences in the epigenetic regulation of the genome" (Forger 2016). So, epigenetics is likely to be involved in sex differences in animals with different sex chromosomes (Forger 2016). Experimental studies in this area have tended to use rats. For instance, Kurian et al (2008) altered the expression of a particular gene in the neo-natal brain, and reduced the normally seen sex differences in juvenile play (ie: male rats play more than females).

Other recent research "suggests that males and females may use different epigenetic mechanisms to achieve the same outcome in terms of gene expression" (Forger 2016).

1.1.2. Testosterone

Testosterone generated from the testes soon after birth ("mini-puberty") is "responsible for establishing sexually dimorphic brain circuitry that controls sexually differentiated behaviours and reproductive physiological processes in several species" (Clarkson and Herbison 2016 p1). Subsequently, testosterone levels drop until the onset of puberty, when another increase in testosterone leads to secondary sex characteristics and adult reproductive function.

But, in primates, brain sexual differentiation occurs with exposure to testosterone in the womb, and the function of the neo-natal testosterone surge in humans is

[2] Heart attack-related.

[3] The sex chromosomes in birds are ZZ in males and ZY in females.

unclear. It is probably related to some aspect of brain sexual differentiation (Clarkson and Herbison 2016).

Particularly with studies of rats, there is interest in establishing the mechanisms involved in the male neo-natal testosterone surge (Clarkson and Herbison 2016).

Animal studies of the biological basis of sexual differentiation, include, for example, Phoenix et al (1959), who administered testosterone in the neo-natal period to female guinea pigs who became irreversibly masculinised. While blocking the neo-natal testosterone surge in different primates has different effects - eg: castrated rhesus monkeys show normal adult sex behaviours, but such male tamarins and marmosets have decreased mounting behaviour (Clarkson and Herbison 2016).

Sex differences in gene expression have been found, and in males adult testosterone is involved, but not adult ovarian hormones in females (Bayless and Shah 2016).

1.1.3. Brain Areas

Bayless and Shah (2016) stated: "Sexually reproducing animals exhibit sex-typical displays of social behaviours, such as mating and aggression. Such sexual dimorphisms in behaviour can be qualitative or quantitative in nature, and they arise from sexually differentiated neural circuits, which in turn are shaped by the varying hormonal, genetic and epigenetic environments of males and females during development and adulthood" (p1). Knowledge about these neural circuits is growing with the use of transgenic/knockout mice, for instance. Knockout mice have a gene deleted or functionally disabled to see the effect. For example, male mice with knockouts for certain genes related to perceiving pheromones showed abnormalities in mating and male-male aggressive behaviours, and this normally interacts with testosterone (Bayless and Shah 2016).

Gorski et al (1980) were the first to report sex differences in the rat brain in the sexually dimorphic nucleus (SDN) of the pre-optic area, namely that it is larger in males than females. Knowledge about the function of this area, however, "remains elusive" (McCarthy 2016).

Studies that have experimentally altered the SDN (or sometimes called INAH-3) with hormones in animals have changed sexual orientation.

"Common portrayals of hormone-mediated sexual differentiation imply that males are exposed to high levels of gonadal steroids, whereas females see none. But

in reality, the level of hormones does not differ all that greatly in brain tissue, and in some regions that are sexually differentiated, the levels of steroid do not differ at all between males and females. Moreover, if males are injected with a dose of steroid that would masculinise a female, there is no greater masculinisation seen in those males. Thus, something acts as a governor both to prevent females from being masculinised by their own steroids (levels of which are lower than in males but still present) and to keep males from being super masculinised when steroid levels are exceedingly high" (McCarthy 2016 p7).

1.2. HUMANS

Using diffusion magnetic resonance imaging (MRI), Tunc et al (2016) found differences in connections in different brain areas while performing fourteen cognitive tests - males more connectivity in motor, sensory and executive areas, and females in areas related to social motivation, attention, and memory tasks. Males had higher connectivity of neurons within areas of the brain, while females had higher connectivity between areas. The data came from the Philadelphia Neurodevelopmental Cohort which includes 900 teenagers and young adults.

McCarthy (2016) stated what she called the "logical truism" that "human brain and behaviour are far more complex and more profoundly influenced by environment and experience than commonly used animal models at every level, meaning fish, reptiles, birds, rodents and non-human primates" (p2) (appendix 1A).

She also warned that there is "the pervasive assumption that a sex difference in neuroanatomy or neurophysiology is synonymous with a sex difference in behaviour. Rather than an assumption, the connection between anatomy and behaviour should be a hypothesis subject to empirical testing. In the case of human imaging studies, there is concern of pervasive reverse inference in which sex differences in fMRI [functional magnetic resonance imaging] signal are interpreted as empirical evidence of pre-existing stereotypes, rather than actually tested" (McCarthy 2016 p2).

Another issue is the level of analysis: "Studies relying on global imaging techniques such as MRI [magnetic resonance imagining] in humans versus gene expression profiles or biochemistry in animal models are profoundly different in both technical and experimental fidelity. In the first instance, a neuroscientist may be attempting to understand language processing, whereas the latter is exploring a protein that resides at the synapse. Each has their own strengths and weaknesses, but

neither the strengths nor the weaknesses are transferable. Moreover, results based on one level of analyses do not allow for sweeping conclusions" (McCarthy 2016 p3).

There is a "notion of the brain as a unitary organ that is either 'male' or 'female'. Because the majority of sex differences in the brain are established early by gonadal steroids that differ in males and females, and because the brain resides in a body that is either male or female, there is an implicit, even inherent bias, that brains are male versus female" (McCarthy 2016 p2).

"Volumetric sex differences" studies concentrate on "an area, nucleus, cell layer or fibre track... found to be bigger in one sex" (McCarthy 2016). Initially, this was done in post-mortem histological analyses, but such studies "can be assumed to include very few healthy controls" (McCarthy 2016). Neuroimaging studies have allowed researchers to observe living brains, but the studies need interpretation of the statistical approaches and algorithms used (McCarthy 2016).

McCarthy (2016) pointed out that some people "argue it is folly to study neuroanatomical sex differences with the hope of understanding sex differences in behaviour as the connection between anatomy and behaviour is often weak or even non-existent" (p5). She suggested that "sex differences in behaviour are loosely tethered to neuroanatomy" (ie: anatomy "exerts some constraining influences, but the behavioural output is subject to buffering from numerous extraneous influences"; McCarthy 2016 p6) (appendix 1B).

One area of research that appears robust is of children's toy preference (McCarthy 2016). While girls exposed pre-natally to more testosterone due to the genetic condition congenital adrenal hyperplasia (CAH) [4] have a "boy-like toy preference" (eg: Lamminmaki et al 2012; Pasterski et al 2005). Hines et al (2016) (appendix 1C) argued that "CAH girls are less sensitive than unaffected girls to extraneous socialisation cues about gender-appropriate toy choices. Thus, rather than concluding that there is some undiscovered 'prefers-dolls-nucleus' in the brain, her recent work demonstrates how children are differentially sensitive to socialising cues, so that girls become even more girl-like by modelling the behaviour of other females. In this way, the nature versus nurture conundrum is broken down with

[4] CAH is classed as a disorder of sexual development (DSD) where children are born with "intermediate genitalia" - ie: "an overlarge clitoris, an undersized penis or features of both sexes" (Reardon 2016). Other DSD include XY individuals who female due to mutations in the SRY gene or individuals with the SRY gene but no Y chromosome (Reardon 2016).

the realisation that nature determines the response to nurture. Whether the converse is true for boys is not yet known" (McCarthy 2016 p4).

McCarthy (2016) observed: "The most polarised views on sex differences in humans are understandably centred around cognitive aptitude and abilities. This is appropriate as we should never easily accept a scientific conclusion that could be used to justify discrimination or limit opportunities for one sex [5]. No matter how often we repeat that different does not mean better, there is always a tendency to conclude that certain skill sets are superior over others. A good exercise to gauge how divisive a finding of sex differences associated with cognition can be is to substitute the word 'race' for 'sex'. However, honest evidence-based debates on sex differences in cognitive regions of the human brain should be limited to just that, cognition, and not used to conclude there are no differences in the brains of human males and females" (p4) [6].

1.2.1. Sexual Orientation

The organisational/activational hypothesis emphasises the early exposure of testosterone in males, and oestrogen and progesterone in females as the basis of sexual behaviour. Altering these hormones can change partner preference.

Bakker et al (1993) inhibited testosterone in male rat embryos and pups, and found such individuals showed female sexual behaviour as adults (eg: allowed males to mount them). Henley et al (2009) found the equivalent in female rats where oestrogen was inhibited in the first three weeks of life.

Spontaneous homosexual behaviour has been systematically observed in a population of male sheep in Idaho, where 8% of rams are male-oriented rams (MOR) (ie: no sexual reaction to females) (Perkins and Roselli 2007). These males have an area of the brain (ovine sexually dimorphic nucleus of the pre-optic area; oSDN) of similar size to females. Normally, the male oSDN is

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[5] There are a number of ideas in society that used to restrict female behaviour (appendix 1D).

[6] Compensation or convergence refers to "the phenomenon in which the two sexes find a different way to solve the same problem. This may involve different anatomical substrates in males and females for purposes of convergence on the same behaviour... A combination of compensation and convergence is found in spatial maze learning. Under some conditions, males consistently outperform females, but in others, the reverse is true, and this appears to be largely dependent upon the learning strategy employed. Males and females attend to different cues (geographic versus local) when solving the maze, but as long as both types of cues are equally available they solve the task equally well" (McCarthy 2016 pp6, 7).

three times larger. The difference is a result of exposure to testosterone in the womb (Balthazart 2016).

Experiments with rats have shown that the early environment can influence sexual behaviour. For example, male rats raised with almond-scented males developed a sexual preference for these individuals over unscented males or females (Triana-Del Rio et al 2011).

How applicable are biological theories of sexual behaviour based on studies with rats to explaining human homosexual behaviour? [7] Because experimental manipulation of the hormones in the womb is not possible, indirect measures of difference in testosterone, say, are sought. For example, the relative length of the index to the ring finger (which is shorter in lesbian than straight women), or the suprachiasmatic nucleus (larger in gay than straight men) (Balthazart 2016).

But Balthazart (2016) highlighted three key limitations of such measures:

- "some of these effects have been reproduced, but others have not and the origin of the discrepancies has not always been identified";

- "although statistically significant, the differences observed only explain a part of the variance";

- "it is sometimes unclear whether the difference observed reflects the signature of a differential early exposure to steroids and is potentially a cause of homosexuality or if it is a consequence of this sexual orientation" (p6).

There are pathological conditions that change the embryonic endocrine environment, like congenital adrenal hyperplasia (CAH), where girls are exposed to high levels of testosterone. As many as 40% of such females show homosexuality (compared to 10% in the general population) (Balthazart 2016).

Yet the majority of CAH women are heterosexual, so other factors must be involved in sexual orientation. Genes, for instance. Balthazart (2016) stated: "Overall,

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[7] Sedgwick (1990) challenged the binarism behind the heterosexual/homosexual distinction: "It is a rather amazing fact that, of the very many dimensions along which the genital activity of one person can be differentiated from that of another (dimensions that include preference for certain acts, certain zones or sensations, certain physical types, a certain frequency, certain symbolic investments, certain relations of age or power, a certain species, a certain number of participants etc etc etc), precisely one, the gender of object choice, emerged from the turn of the century, and has remained, as *the* dimension denoted by the now ubiquitous category of 'sexual orientation'" (p8). Rubin (1975) referred to the "sex/gender system" - "the system by which chromosomal sex is turned into, and processed as, cultural gender" (Sedgwick 1990).

data suggest that in social conditions typical of Western societies, about 50% of the variance in human sexual orientation has a genetic origin [...] these studies leave no doubt about the existence of genetic controls on sexual orientation, but at the same time they show that these controls are likely to be polygenic and very complex" (p7).

Epigenetics is another possible factor in sexual development. For example, the same gene may respond differently on the X than Y chromosome (Balthazart 2016).

1.3. ANIMAL STUDIES

Shors (2016) reviewed the studies on sex differences in learning in rats, and highlighted issues relevant to understanding sex differences generally.

It has been found that male rats show improved associative learning (ie: classically conditioned responses) under stressful conditions compared to no stress, while female rats have the opposite pattern. Males castrated at birth do not show any difference in learning as adults.

But when females used in experiments were ovariectomised (ie: ovaries removed in adulthood), or injected with testosterone immediately after birth, they showed the same improvement as males. Also females caring for offspring, and virgin females caring for another female's offspring. In fact, "females that had been mothers at some time in their lives were likewise resilient to the negative effects of stress, even when they were no longer taking care of their offspring (long after weaning)" (Shors 2016 p5).

Traditionally, animal experiments have used virgin females, but, Shors (2016) stated, it is "self-evident... that most adult females in our world, irrespective of species are not virgins".

Shors (2016) noted care when studying sex differences in animals in the laboratory - "For example, female rodents are typically more physically active than male rodents. Therefore, investigators who rely on measures of activity (such as those measuring conditioning, learned helplessness, fear, etc) must consider the possibility that observed sex differences in 'learning' or 'depression' are not necessarily reflecting these complex psychological constructs but are rather attributable to differences in performance" (p9).

Male adult rats are larger than females, and Shors (2016) drew two points out:

a) A comparison of brain size is unhelpful - "For example, the absolute number of new neurons in the adult

hippocampus of the female are significantly fewer than in males and therefore, measurement differences must be assessed according to density of cells rather than absolute numbers, and even this might not always be a suitable alternative" (Shors 2016 p9).

b) Weight differences produce differences in behaviour - For example, "pairing an adult male rodent with a female rodent produces aggressive behaviours towards the female. The male is able to subjugate the female, at least in part, because he is larger in size. However, the female is also better able to escape, because she is smaller and more agile. Without the sex differences in size, the sex differences in behaviour might not even occur" (Shors 2016 p9).

1.4. RECENT CONTROVERSY ON BRAIN DIFFERENCES

Joel et al (2015) looked at over 1400 brain scans of individuals aged between 13 and 85 years, and identified a number of brain regions that varied depending on whether the person was male or female. Only 8% of the sample had "all-male" or "all-female" brains (ie: consistency across the differences) (Hamzelou 2015).

Four data-sets of MRI images were used:

- From Tel-Aviv University: 169 women and 112 men; 10 regions of grey matter volume showed the largest sex differences, and were focused upon out of 116 possibilities.

- From University of Zurich: 69 women and 69 men; 11 regions out of 116.

- From "1000 Functional Connectomes Project": 495 women and 360 men; same as Tel-Aviv sample.

- Nathan Kline Institute sample: 167 women and 100 men; 12 areas of focus out of 168 cortical regions, and white and grey mater.

Joel et al (2015) summed up: "Our study demonstrates that although there are sex/gender differences in brain structure, brains do not fall into two classes, one typical of males and the other typical of females, nor are they aligned along a 'male brain–female brain' continuum. Rather, even when considering only the small group of brain features that show the largest sex/gender differences, each brain is a unique mosaic of features, some of which may be more common in females compared with males, others may be more common in males compared with females, and still others may be common in both females

and males. The heterogeneity of the human brain and the huge overlap between the forms that brains of males and brains of females can take can be fully appreciated when looking at the entire brain" (p15472).

Del Giudice et al (2016) performed further analysis of Joel et al's (2015) data, and found that "brain features correctly predicted subject's sex about 69-77% of the time" (pE1965). They also criticised the process of dividing the scans into groups based on internal consistency. Applying this technique to distinguishing facial morphology of three species of monkeys, the researchers found little internal consistency. They stated: "If the methods of Joel et al (2015) cannot demonstrate consistency in morphological features that distinguish distinct species, is it any wonder that they cannot demonstrate within-individual consistency in sexually differentiated brain structures and behaviours in humans?" (Del Giudice et al 2016 pE1965).

Rosenblatt (2016) criticised the statistical analysis used by Joel et al (2015), which could produce a situation where two groups are not distinct when compared on one variable, but are on two variables ("univariate overlap with multi-variate separation").

Chekroud et al (2016) reported that sex differences could be distinguished from whole-brain patterns using over one thousand MRI scans publicly available. They observed that "the human brain may be a mosaic, but it is one with predictable patterns" (pE1968).

Glezerman (2016) criticised the use of the "still images" of MRI as "akin to examining a road map and drawing conclusions about traffic patterns". The differences in the brain are functional not morphological (or structural), they argued. Joel et al (2016b) defended themselves by pointing out that brain function and structure were assessed in their original study. Brain function (as seen in personality characteristics, for example) showed that "there were many more people with both 'feminine' (ie: more common in females compared with males) and 'masculine' (ie: more common in males compared with females) characteristics than people with only feminine or only masculine characteristics" (pE1972).

Generally, in their defence, Joel et al (2016a) stated: "Clearly, sex affects the brain, as evidenced in differences between brains from females and brains from males in both macroscopic and microscopic features. However, the fact that sex affects the brain does not necessarily entail that there are two distinct types of brains, 'male brains' and 'female brains', as there are two distinct types of genitalia" (pE1969).

They also defended their methodology to the criticisms of Del Giudice et al (2016), Chekroud et al (2016), and Rosenblatt (2016) by pointing out that differences in datasets, and variations in statistical models produce different findings (eg: "correcting" for differences in brain size or not).

Joel et al (2016b) summed up: "There is no doubt that sex affects the structure and function of brain cells. However, the fact that sex can affect brain cells does not necessarily entail that the form and function of brain cells are either 'male' or 'female' nor that the brains comprised of these cells can be divided into two distinct categories" (pE1972).

1.5. OTHER PHYSIOLOGICAL DIFFERENCES

Differences between the sexes are usually seen in relation to reproduction, but there are differences in many parts of the body. For example, the mid-gut (similar to the small intestine) of the fruit fly (Drosophilia melanogaster) is longer in females, especially after mating, which is "regulated by a previously unidentified branch of the sex-determination pathway" (Fear and Oliver 2016 p289). A longer gut would aid absorption of nutrients from food, and the eggs produced by the female need proteins and lipids.

Hudry et al (2016) investigated the genes involved in experiments which included masculinising females, who did not show the mid-gut expansion after mating of normal females.

Put simply, the intestinal stem cells (involved in the expansion of the mid-gut) have a "sexual identity".

1.6. APPENDIX 1A - CONCERNS WITH REPORTING HUMAN SEX DIFFERENCES

Maney (2016) observed: "The idea of sex differences in the brain both fascinates and inflames the public. As a result, the communication and public discussion of new findings is particularly vulnerable to logical leaps and pseudoscience" (p1). The Internet is full of "an alarming amount of pseudoscience" on information-based websites, including that women listen with both sides of the brain while men use only the left side, and women have more white matter and men more grey matter (Maney 2016).

Maney (2016) described three fallacies that make communicating sex differences problematic:

1. For any trait or behaviour, the sexes are either different or the same.

In reality, most traits and behaviours overlap, but the "conceptualisation and communication of that overlap are impeded by our natural urge to dichotomise and by language choices that emphasise difference. [...] The problem here is that we are asking a yes-or-no question when both 'yes' and 'no' are the wrong answer. To truly understand the nature of most sex differences, which arguably are not actual 'differences', we need to ask how much the sexes differ, not whether or not they do" (Maney 2016 p2, p3).

Dividing groups based on sex for analysis "encourage dichotomous thinking about the results", and, in terms of statistics, "dividing a sample into sub-groups lessens power and therefore the ability to detect effects" (Maney 2016). To make such a point, Sleight (2000) analysed data on daily aspirin intake and heart attacks by sub-groups of astrological sign. Overall, the data showed a clear benefit, but this was not the case for the Libra and Gemini sub-groups. "Testing a hypothesis within each sex incurs a similar risk that an effect will be detected in one sex but not the other, when in fact both sexes are responding" (Maney 2016 p7).

Similarly, Joel and Fausto-Sterling (2016) stated: "In the study of variation in brain structure and function that might relate to sex and gender, language matters. It matters because the choice of words and the meanings behind them frame our research questions and methods. And it matters because inconsistent or imprecise use engenders confusion" (p1). For example, McCarthy and Konkle (2005) distinguished between sex dimorphism and sex difference. The former, they argued, refers to aspects of difference that "truly come (or nearly so) in just two forms" (eg: X and Y chromosomes, genitalia) (Joel and Fausto-Sterling 2016). Sex dimorphism is not applicable when referring to the brain, McCarthy and Konkle (2005) pointed out.

However, Joel and Fausto-Sterling (2016) observed: "While some newer scientific work seems to have dropped the use of dimorphism or reference to male versus female brains, instead referring to human brains, the use of the word dimorphism to describe sex-related brain differences appears in the scientific literature frequently and seemingly without critique. Matters are far worse in popular renditions of scientific findings. These routinely portray brain differences as dimorphic, uncritically comparing 'male brains' to 'female brains' (as opposed to comparing brains from males to brains from females)" (pp1-2).

Joel and Fausto-Sterling (2016) argued for the "mosaic brain hypothesis", which "pulls us outside the dimorphism-difference formulation". Simply, this hypothesis describes "a brain that has one component in

the form more typical of females... and one component in the form more typical of male..." (p2) [8].

The apparent reversal of sex differences can be used as evidence for the mosaic brain hypothesis. One study with rats (Reich et al 2009) found that prolonged stress changed the density of an area of the hippocampus. In non-stressed rats, females have low density and males high density of neurons, but after stress this was reversed. This is a sex-by-environment interaction (Joel and Fausto-Sterling 2016).

2. The cause of a sex difference can be inferred from neuroanatomy (ie: brain differences).

This is a false cause fallacy, and Maney (2016) gave this example: "(i) the hemispheres of the brain are more heavily interconnected in women than in men; (ii) greater hemispheric interconnectedness allows better multi-tasking; (iii) women are better multi-taskers than men, therefore the anatomical difference explains the difference in ability. First, the evidence that variation in inter-hemispheric connections actually contributes to variation in human abilities is practically non-existent. Second, studies of multi-tasking have shown no female advantage. The argument pervades popular culture nonetheless, probably because it appears to confirm stereotypes" (p3).

The reporting of science in the media is based on "newsworthiness", and a study finding an overlap between the sexes is thus not viewed as interesting. But a clear sex difference is "more meaningful to the public", particularly if the "researchers are prone to speculate about the functions of those differences" (Maney 2016).

Differences in brain structure of males and females do not necessarily mean differences in function. There is a principle of "compensation" (eg: De Vries and Boyle 1998) - ie: "sex-dependent processes that act to reduce rather than create differences between females and males" (Joel and Fausto-Sterling 2016).

"Yet, when scientists and laypeople list differences between females and males in the brain, they often

[8] Joel and Fausto-Sterling (2016) said: "We believe that current data are better explained by the assumption that human brains belong to a single heterogeneous population rather than to two distinct populations. If this is so, then using sex category as a variable is both unnecessary and misleading. Comparing brains of females to brains of males would be analogous to comparing two samples randomly drawn from a single population of brains, rather than to comparing two samples, one randomly drawn from a population of ‘male brains’ and the other from a population of ‘female brains’. As a result, although such comparisons may well yield significant differences between females and males (due to the high heterogeneity of the population), these differences would probably reflect a false-positive finding resulting from a chance difference between the two samples included in a specific study" (p4).

implicitly assume that the more differences there are, the more different are the two sex categories, ignoring the possibility that some – possibly many – differences may compensate for others" (Joel and Fausto-Sterling 2016 p3).

Maney (2016) provided this example of how science reporting is extrapolated beyond the actual findings. A study with mice (Farmer et al 2014) found that females experiencing pain spent less time with males, but males in pain were still interested in females [9]. "In their paper, the authors argued that the findings 'suggest that the well-known context sensitivity of the human female libido can be explained by evolutionary rather than socio-cultural factors'... The press release, which led with 'Not tonight honey...' proved irresistible; the study received worldwide coverage. The fact that it was conducted in mice, not humans, was sometimes lost, however. Headlines announced, 'Women's low sex drive due to biological reaction to pain' and 'It's science: why your headache excuse is actually legit but his isn't'. The coverage of this study shows clearly that animal studies are not immune to widespread media attention or potential over-interpretation" (Maney 2016 p7).

3. Sex differences in the brain are innate and fixed.

Terms like "hardwired", "natural", or "genetic" are often used in reference to sex differences, and Maney (2016) felt that "these terms are nearly always used to argue that sex stereotypes are rooted in biology. They make sex differences sound predetermined and inevitable, untouched by experience or culture" (p3). The brain is plastic and experience plays a key part in development.

1.7. APPENDIX 1B - BIRDSONG

In terms of clear brain sex differences, songbirds are a well-studied example, and, in particular, the size of the forebrain song-control nuclei [10]. Such areas are larger in males and females (eg: zebra finches, canaries) (Ball 2016) [11].

Early studies concentrated on males and tried to establish a link between the size difference between the

[9] Mogil (2016) emphasised that studies showed that women are more sensitive to pain and less tolerant of it than men. This may be because rat studies have found that males and females process pain through different immune cells in the spinal cord (microglia in males and T cells in females) (Sorge et al 2015).

[10] Hyperstriatum ventrale pars caudale (HVC) (Ball 2016).

[11] In some species (eg: marsh wrens), females do not sing, whereas others do in duets with males (Ball 2016).

sexes of the song nuclei and the repertoire of the male song, for instance (eg: larger difference in size goes with sophisticated song). Nottebohm et al (1981), for example, compared forty-six male and female canary brains, and found that size of the song nuclei was related to repertoire size. While Canady et al (1984) found that male marsh wrens (Cistothorus palustris) on the east coast of the USA had larger song nuclei volumes and song repertoires than marsh wrens elsewhere in North America.

Does that mean the co-evolution of sex differences in the brain and in singing behaviour? This idea is supported by data from molecular genetics (Ball 2016).

On the other hand, there are species, like the African bush shrike (Laniarius funebris), where males and females have similar song complexity, yet the male song nuclei is still larger (Ball 2016).

Ball (2016) offered these possibilities: "It could be that a basic song system evolved in males and females to support learned vocal behaviour and that the sex differences observed evolved because of male and female specialisations in vocal behaviour [12] that are not related to sexual selection per se" (p6). Or "that males in avian species tend to have higher concentrations of circulating testosterone in the blood than females and these higher concentrations of testosterone tend to promote larger song nuclei" (Ball 2016 p7).

1.8. APPENDIX 1C - HINES ET AL (2016)

Between 3 to 11 years old, gender differences in toy preference have been confirmed with boys preferring toy vehicles and guns, and girls dolls and tea sets (Hines et al 2016). These differences are not purely biologically-based, but are influenced by socialisation (eg: parents encouragement of gender-consistent toy choices).

Hines et al (2016) pointed out that "once children understand that they are girls or boys, they tend to model, or imitate, the object choices and other behaviours of individuals of the same sex more than those of individuals of the other sex. They also respond to gender labels, preferring objects, including toys and activities that have been labelled as appropriate for their own sex over those that have been labelled as appropriate for the other sex" (p2). Responding to appropriate gender models and labels is self-socialisation.

[12] "In the duetting plain-tailed wren (Pheugopedius euophrys), males and females have auditory cells in the song system that are tuned to the joint song the two sexes produce rather than just male or female components" (Ball 2016 p1).

Modelling is studied in experiments by children observing men and women consistently choosing gender-neutral objects (eg: men pick square shape and women triangle) before being offered the objects themselves. Similarly, labelling experiments describe gender-neutral objects as "for boys" or "for girls", and then allow the children to choose.

Girls with CAH are less likely to play with girl-typical toys and more likely to play with boy-typical toys than non-CAH girls. CAH can produce changes in the genitals such that the individuals are classed as boys [13], and such boys do not show any differences in toy preference to other boys (Hines et al 2016).

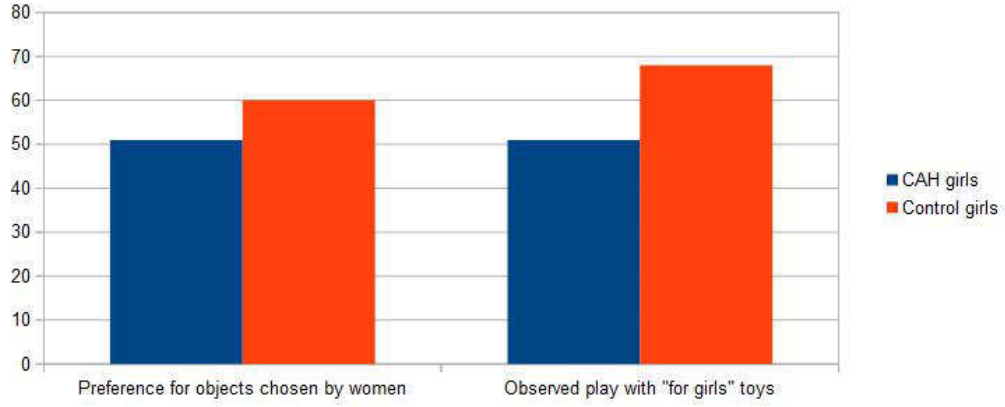
Hines et al (2016) reported their modelling and labelling experiments with children aged four to eleven years old in the UK, of which 43 were CAH girls, 38 CAH boys, 41 unaffected females, and 31 unaffected males.

In the first experiment, the children were shown four gender-neutral objects, and told that two were "for boys" and two "for girls". The two objects chosen in each case was varied between children. The objects were balloons (green and silver), and xylophones (orange and yellow). The children were later left in a playroom for five minutes with all the objects. Girls with CAH showed significantly less choice of "for girls" toys than control girls, but CAH and control boys did not differ in their choice of "for boys" toys.

In the second experiment, the participants watched a video of four adult males and four adult females choosing one object from a gender-neutral pair (eg: men chose pen and women chose pencil). The children were later offered a choice of the objects they had seen on the video. The CAH girls had non-significantly less preference for objects chosen by women than control girls, but the CAH and control boys showed no difference.

Hines et al (2016) concluded: "Our observation of differences in girls with CAH (figure 1.1), but not boys with CAH, increases the likelihood that the effects were caused by elevated androgens, rather than other aspects of the CAH condition, such as cortisol abnormality [...] Our results suggest that processes involved in self-socialisation of gender-related behaviour also are altered in girls with CAH" (p8).

[13] Individuals with CAH are XX but with ambiguous genitalia. Around 90-95% identity as female (Reardon 2016).



(Data from Hines et al 2016 table 2 p5 and table 3 p6)

Figure 1.1 - Percentage of girls.

1.9. APPENDIX 1D - IDEAS THAT RESTRICT WOMEN

The idea of the "biological clock" for women wanting to have children is presented as an accepted "fact" of the modern world (eg: McKaughan 1987). Weigel (2016), however, highlighted the "idea of the biological clock has as much to do with culture as with nature. And its cultural role was to counteract the effects of women's liberation" (p26).

Statistics are quoted that show that women find it harder to get pregnant in their 30s, for instance. But such data can be based on women with fertility problems who seek help (Weigel 2016).

Weigel (2016) stated: "Women and men are found to experience fertility problems at roughly equal rates, but you would never know it from reading most press coverage of the subject. Our assumption seems to be that reproduction is a female responsibility first and foremost. Anything going wrong with it must be a woman's fault" (p26).

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2. RODIN AND LANGER (1977): WHAT REALLY HAPPENED

Rodin and Langer (1977) followed up the field study by Langer and Rodin (1976) (appendix 2A) on the positive effect of perceived control.

Langer and Rodin (1976) divided older adults living in a nursing home into two groups. One group received a talk from the home manager emphasising responsibility for themselves, and offering the residents the choice of plants to care for (responsibility condition). The other group received a talk that emphasised the staff's responsibility for the residents. These residents were given plants that were watered by the staff (comparison condition). The former group "became more active and reported feeling happier than the comparison group of residents" (Rodin and Langer 1977 p897) [14].

Ninety-one individuals had taken part in the original study, of which Langer and Rodin (1976) focused on fifty-two, and Rodin and Langer (1977) found thirty-four of them (ie: 20 from the responsibility group and 14 from the comparison group). Nine individuals who had not taken part originally were added as a control group.

The outcomes were measured by nurses' ratings of mood, awareness, sociability, and mental and physical activity, by medical records, and self-completed questionnaire. The nurses' ratings were added into a composite score at eighteen months after the original talk.

The participants in the responsibility group had a significantly higher mean composite score (figure 2.1), and individual mean ratings than the other two groups (figure 2.2). They also showed an improvement in health, while the other two groups had a decline in eighteen months, and a lower death rate. Thus, the original talk "did indeed produce strong effects that lasted as long as eighteen months later" (Rodin and Langer 1977 p901).

However, this was a field study (ie: quasi-experiment rather than experiment), which meant that many variables were not controlled. These included:

i) No randomisation of individuals to original talk type. The groups were divided for convenience - by floor of the nursing home.

ii) There was no no-treatment control group

[14] The comparison group experienced learned helplessness, with a lack of control, which is linked to depression and negative health experiences.

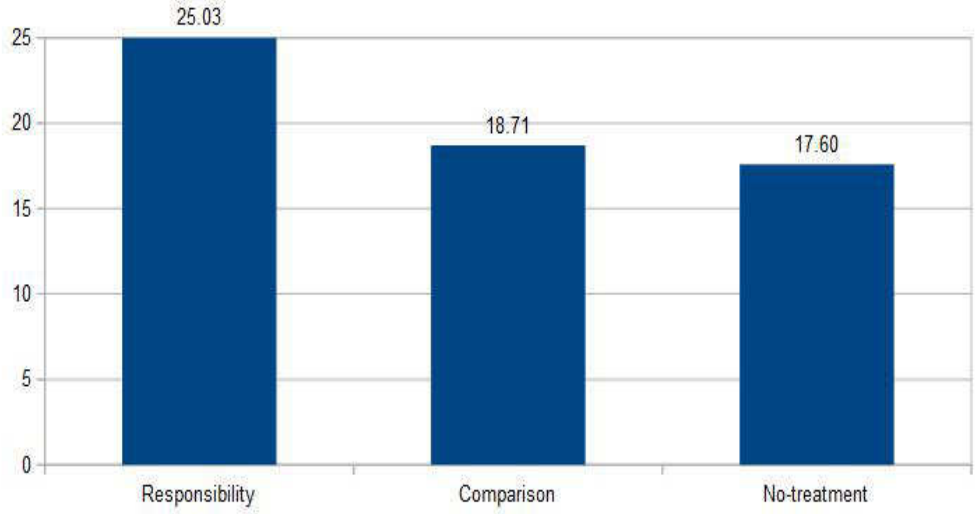
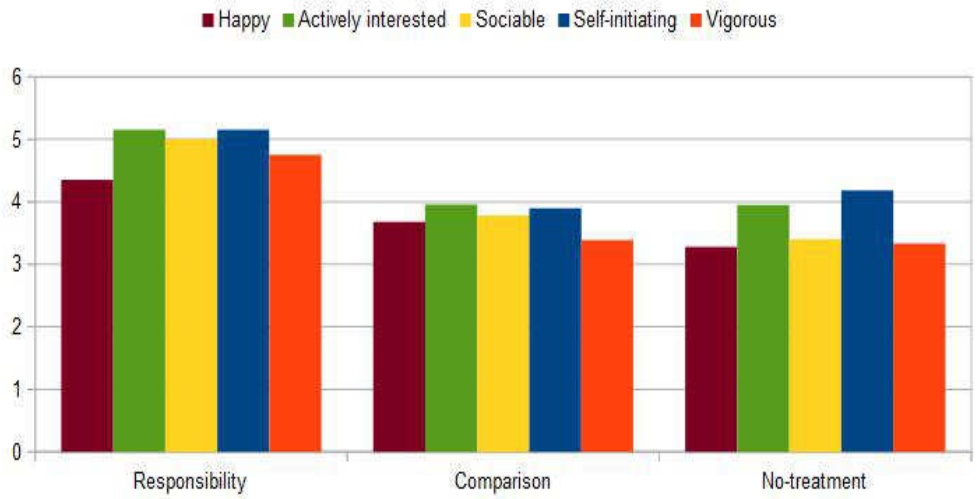


Figure 2.1 - Mean composite scores of nurses' rating at 18 months follow-up.



(Data from Rodin and Langer 1977 table 2 p899)

Figure 2.2 - Mean individual nurses' ratings at 18 months follow-up.

originally.

iii) The amount of interaction between residents and discussion of the manager's talks.

iv) The behaviour of the nurses, and the nurse-resident interactions. Though the nurses were not aware of the study conditions, they were asked to measure

behaviour, which may have changed their behaviour. "In addition, once the patients began to change, the nurses must have responded favourably to improved behaviour, sociability, and self-reliance" (Rodin and Langer 1977 p901).

v) The choice of nursing home in Connecticut, USA, for the study. Rodin and Langer (1977) admitted that "this particular nursing home was open and primed to be responsive" (p902).

APPENDIX 2A - NON-EQUIVALENT CONTROL GROUP DESIGN

Langer and Rodin (1976) is a quasi-experiment, of the type known as a non-equivalent control group design(figure). It may not be possible to randomise the participants, or have matched groups, or treat the conditions the same. In this study, circumstances dictate the make up of the groups being used (ie: no random assignment to conditions) (Brewer 2002).

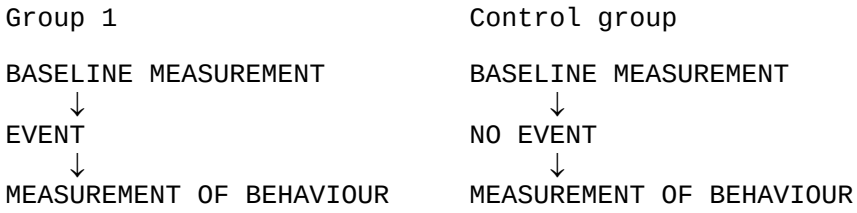


Figure 2.3 - Non-equivalent control group design.

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3. CHILDREN'S MEDICATION DOSING ERRORS

Unintentional medication errors are mistakes in dosing that an individual does not plan (as opposed to deliberate overdosing, for instance). Inappropriate dosage my be due to poor medication packaging. For example, it is estimated that parent dosing error rates may be up to 40% (Yin et al 2016).

Medications for children are more likely to be oral liquid formulations, and the challenges for parents administering these include finding an appropriate tool to measure the dose (eg: oral syringe, dosing cup, kitchen spoon), and the unit of measurement (eg: teaspoon, tablespoon, millilitre), "along with their associated abbreviations, are used as part of instructions on labels and dosing tools, contributing to confusion and multi-fold errors" (Yin et al 2016 p2).

Dosing cups, often provided with over-the-counter medications, for example, are associated with higher rates of parent errors than oral syringes (Yin et al 2016).

In relation to the unit of measurement, Yin et al (2010) found a mismatch between the label and the dosing tool in 90% of top-selling over-the-counter child medications in the USA. One-third of prescribed products have also been found to have different units on the label as compared to the prescription (Yin et al 2014).

Yin et al (2016) found a high level of dosing errors by parents in an experiment [15] at three clinics in the USA. Over 2000 parents of children under eight years old, who agreed to participate, were randomly assigned to one of five groups, which varied in the units on the bottle label and the dosing tool (table 3.1).

Each participant was asked to measure three amounts (2.5, 5, and 7.5 mL) with three dosing tools (10 mL capacity syringe with 0.5 mL increment markings, syringe with 0.2 mL markings, and 30 mL dosing cup). The instruction given was: "Please use this [DOSING TOOL HANDED TO PARENT] to show me how much medicine the label tells you to give the child each time you give the medicine".

Only 0.7% of participants measured out the exact dose correctly. A dosing error, which was defined as greater than 20% more or less than the dose, was made overall by 84.4% of parents. Overdosing was more common than underdosing. Overall, there were more errors with cups than syringes (figure 3.1). Yin et al (2016) explained this finding thus: "the same distance along the

[15] Part of the SAFE Rx for Kids study (Safe Administration for Every Prescription for Kids).

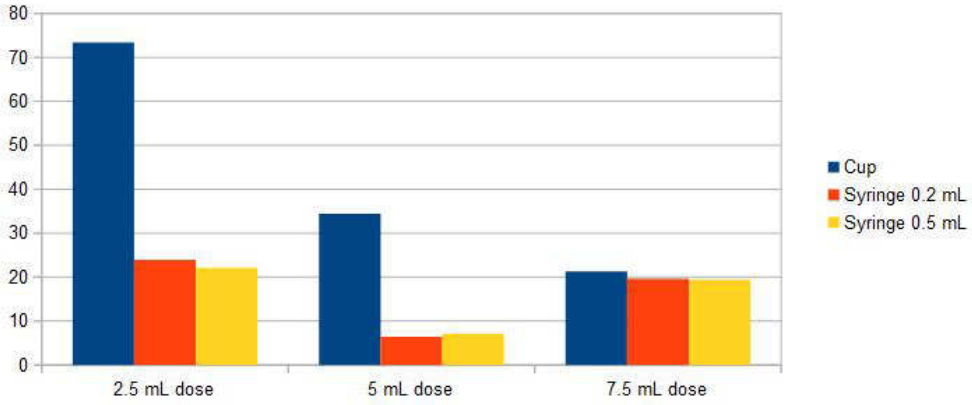
Group	Bottle label	Dosing tool units	Example
1	mL	mL	5 mL (fully matched)
2	mL & tsp	mL & tsp	5 mL (1 tsp) (fully matched, abbreviation)
3	mL & teaspoon	mL & tsp	5 mL (1 teaspoon) (partial match)
4	mL	mL & tsp	5 mL (not matched)
5	teaspoon	mL & tsp	1 teaspoon (not matched)

(Based on Yin et al 2016 figure 1A p3)

Table 3.1 - Medication labels in five independent groups.

side of the tool represents a greater volume for cups than for syringes (eg: for cups, 1 mm might represent 0.8 mL; for syringes, 1 mm might represent 0.1 mL). 27 In addition, when a cup is not held at eye level, it may appear to be filled to a particular marking when it is not" (p8).

More errors were made in group 5 (ie: use of "teaspoon" on the bottle label and "mL (tsp)" on the dosing tool.



(Based on Yin et al 2016 figure 3 p8)

Figure 3.1 - Mean (%) dosing errors by tool type for three different doses.

Yin et al (2016) summed up: "Our findings suggest that health care providers should encourage oral syringe use for the measurement of liquid medications,

particularly when small doses are recommended; this change would probably benefit all families, regardless of health literacy and language. The types of unit of measurement discordance between labels and tools we studied appeared to have a limited impact on error rates, although our findings support avoidance of using teaspoon alone on labels. Notably, even when syringes were used with concordant millilitre only labels and tools, parents made 1 or 2 errors on average across the 9 trials in this experiment" (p9).

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