Stress mechanism is sex-specific: Female amelioration or escape from stress to avoid compromising reproduction contrasts with male utilisation or in effect manufacture of stress to fulfill male 'genetic filter' function

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Research into stress response has exploded in the wake of findings of major sex differences, to show, further, that mechanism is genetically and epigenetically underpinned non-overlapping neuro-hormonal pathway specific to each sex: that is, it is not merely sex-dimorphic but sex-dichotomous; sex-specific. A general principle now appears to emerge of a still more fundamental distinction in stress mechanism than the generally accepted conceptualisation of female 'tend and befriend' vis-a-vis male 'fight or flight'. Stress for the female essentially is a problem because of its negative impact on reproduction, and hence females have evolved to escape stressors through easily registering them in order

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to be motivated to escape; if need be through profound inactivity (major depression). By contrast, stress for males not only is not the problem it is for females, but it usefully drives intra-sexual competition, which males require so as to achieve rank indicating genetic quality – and the stress entailed in contesting and maintaining rank makes it 'honest signalling'. With male ranking determining sexual selection by females, then it is in the service of purging accumulated gene replication error (the fundamental problem for all biological systems): the 'genetic filter' [Atmar (1991)] / 'mutational cleanser' [West-Eberhard (2005)] key function of the male. Consequently, males tend not to try to escape stressors but to live with and to utilise, and even, in effect, to 'manufacture' stress; and thus have evolved a higher threshold to register stress and can attenuate and override it. Sex-specific stress mechanism appears, as would be anticipated, to be a manifestation of the foundational distinction in function between the sexes.

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The recent explosion of research into stress response mechanism has come in the wake of the realisation that there are profound sex differences long entirely missed through experimentation having been conducted only on males (usually mice/rats, but other mammal species as well as humans; stress response being almost identical across mammalia, humans not excluded). This restriction in choice of subjects was because data from females would be confounded by the effects of levels of female sex hormones varying according to the point reached in the oestrus cycle; these hormones themselves impacting on stress response. It was insufficiently appreciated that they may be integral to female stress mechanism, which, therefore, would not be generalisable from data obtained from all-male sampling. Yet it may not have been easily foreseen that stress mechanism would diverge so profoundly according to sex. That the male was considered the default less complicated sex, with female stress physiology 'bolted on', as it were, was far from an unreasonable position, and actually (it has recently been discovered) had scientific validity in that the biology of sex determination is not from a generic female template, as long had been supposed, but a male developmental trajectory which has to be actively suppressed instead for female individuals to be derived [Boulanger et al (2014)].

Somewhat paradoxically upholding the use of only male subjects, the ideological notion that the female functions in no respect in a different (and possibly by implication 'lesser') way than does the male, leads to data from experiments being considered equally admissible irrespective of whether they are from all-male, all-female or mixed-sex sampling. With male same-sex data viewed as being as good as any, then continued use of university students, mostly or almost exclusively male, was not regarded as problematic; until the increasing proportions of female students led additionally to mixed-sex and even female same-sex sampling to produce inconsistent and contradictory data. Even incorporating into experimental design controls for the effects of oestrus cycling so that all-female samples supposedly would be equivalent to those all-male, still did not produce similar results, thereby confirming that female and male stress physiology are not the same, overturning the premise of sex-identicality.

This was seized upon to drive a research programme, still very much ascendant, to discover the basis in stress reactivity of the much higher incidence of major depression in women: a major

focus through an important funding stream stemming from contemporary ideological concern with the female a supposed victim and concomitantly supposedly 'better', built on deep-seated pro-female attitudes arising from the biological stark fact that the female is the limiting factor in reproduction, and equally corresponding deep-seated anti-male prejudices stemming from the biological imperative to control male access to females. The insistence hitherto on male and female identicality is flippable to an insistence on their difference, even to the extent of mutual inversion – reflecting a general perennial oscillation within feminist ideology in vain attempt to reconcile the claim of nil sex difference with the supposition that one sex 'oppresses' the other. Concentrating on female depression has tended to narrow research to looking for gross hormonal changes, to the detriment of an holistic understanding of stress mechanism. Then again, the volume of funding has enabled teams to draw on it for ostensible investigation of female depression whilst actually examining stress mechanism more widely.

In the end, from the perspective of either science and/or current ideology, then, acknowledging and studying profound sex-difference proved inescapable.

In the wake of properly regarding the sexes separately, beginning circa 1995, by 2000 an evidenced sex dichotomy was proposed, based on interpreting endocrinological findings in the light of the evolved divergence of male and female strategic requirements. Ancestrally, females needed to respond to threats by remaining with offspring in mutual support with female non-kin upon female exogamy (moving from the natal group to the male pair-bond partner's community), leaving males to respond actively and to be prepared to take risks in defending their natal group from human and animal-predator attack as well as to hunt large and dangerous game. This evolutionary rationale informed interpretation of data, to give rise to the now well-known conceptualisation of stress in terms of female 'tend-and-befriend' vis-a-vis male 'fight-or-flight' [Taylor et al (2000), well supported subsequently; eg, and most recently by Byrd-Craven, Auer & Kennison (2014)]. The broad endocrinological basis of this had become established two decades ago, before the Taylor theory was formulated; being indeed a basis of it, with oxytocin the key. For females, oxytocin reinforced by oestrogen and other female sex hormones counteracts the negative impact of stress through being a cortisol antagonist; whereas for males, not only does the absence of female sex hormones preclude an amplification of the effects of oxytocin, but the male anyway has comparatively low levels of oxytocin; and, furthermore, these are depressed by testosterone, which instead promotes (argenine-)vasopressin and thereby an actually amplified stress response [Uvnas-Moberg (1997), McCarthy (1995), Jezova et al (1995, 1996)]. Subsequent to Taylor, vasopressin has been found to have profoundly different effect according to sex: in males it underpins agonistic (aggressive) behaviour; for females it promotes affiliative responses [Thompson et al (2005)]; this clearly underlying the 'tend-and-befriend' vis-a-vis 'fight-or-flight' model. The impact of stress is further counteracted, uniquely in women in the inhibition of cortisol secretion by beta-endorphin
[Lovallo et al (2015)]; and also through higher levels, compared to men, of Corticosteroid Binding Globulin (CBG, a.k.a. Transcortin), the protein which binds to and transports cortisol in the bloodstream, resulting in more cortisol becoming tied up and rendered inactive in women [Stolk et al (1996)]. Instead of higher cortisol levels being responsible for stress-induced greater emotional reactivity in females than in males, it is now known to be through lowered levels of the female sex hormone, estradiol [Minni et al (2015)]. This seeming paradoxical state in females of an enhanced registering of stress at the same time as greater dampening down of the impact of stress physiology

is addressed below. The major difference between the sexes in the character of stress mechanism is shown in the overall deleterious impact of stress in multi-systemic wear & tear (allostatic load), which increases with occupational status for men, and actually decreases for women [Juster et al (2013)].

Further than the sex-polarisation envisaged as merely sex- dimorphism in the Taylor model, it is now known (as here outlined) that male vis-a-vis female stress response in the most important respects is non-overlapping: that is, there is not merely sex-dimorphism but sex-dichotomy; sex-specificity. Differences in many respects are not merely separate quantitative ranges of what qualitatively is the same mechanism, but actually different neuro-hormonal pathways according to sex (see below); and even when system elements appear to be the same, or are dissimilar though corresponding to that of the other sex, then changes in response to stress may be in opposing directions; notably regarding hormones. For example, in response to acute stress, both estradiol and testosterone decrease in females, when they increase or are unchanged in males [Lu et al (2015)]; and in response to chronic stress, in the adrenal gland, testosterone receptors decrease in females whilst oestrogen receptors increase in males [Balog et al (2015)] – this relating to the remarkable sex-dichotomy of chronic stress causing obesity in women but weight loss in men. The cascade of findings and scale of interest in stress sex-specificity is indicated by the large number even of just the very recent papers with the terms 'stress' and 'sex-specific' both in the title – about sixty since 2012. Sex-specificity is a most interesting finding, being fully anticipated from key biological principles still more foundational than the evolutionary explanations put forward by and in the wake of the Taylor theory. The mechanisms of how the individual deals with a range of stressors – how stress is either ameliorated or utilised – appears to be a translation at a more proximal level of the foundational facets of complex biological systems.

Why there is more than merely quantitative sex-difference to amount to sex-dichotomy is easily answered by considering the respective functions of the sexes. The central biological problem of how to deal with accumulated gene replication error is the basis of why there is a separate male mating type, to which natural and sexual selection in effect can be quarantined away from females, allowing them to continue unhindered with reproduction. From this male 'genetic filter' [Atmar (1991)] / 'mutational cleanser' [West-Eberhard (2005)] function, it is clear that males are obliged to be intra-sexually highly competitive, in order to achieve sufficient rank in male dominance or prestige hierarchy to thereby advertise genetic quality, which is the criteria by which females assess male attractiveness. Males with 'good genes' are sexually selected by females; and, if particularly high-status, a male is able to serially pair-bond with high-fertility females and attract many others for potential extra-pair sex. Females not only have no use for this – apart from having no 'genetic filter' function, the female cannot benefit from sexual partners in number – but need to avoid competition, given that it can have physical and physiological adverse impacts on their reproductive potential; this being particularly serious in the female, being the sex that is the limiting factor in reproduction. This is just what is seen, as outlined above, with the various ways that cortisol is counteracted in the female. Given that stress cannot all be alleviated, then women have also evolved the facility to directly react to stress in terms of reproductive strategy. They can modify behaviour to be in accord with an environment relatively inauspicious for reproduction, where the reliability and utility of a pair-bond partner is questionable, by more short-term mating behaviour rather than just pair-bonding [Reeve, Kelly & Welling (2015)]; the sex-specific mechanisms underpinning which are known [Toufexis et al

(2013)].

Whereas females need to rid themselves of stress, males can usefully utilise stress as an endogenous means of motivational tension prompting resolution in intense competition to achieve dominance rank as a signal to females of their genetic quality; and, moreover, inasmuch as the stress entailed in such competition is deleterious to the victor through the effects of cortisol and testosterone, this is all to the good in facilitating 'honest signalling' of 'good genes' in male ranking [eg, Muehlenbein & Watts (2010)], thereby furthering still more the male function of 'genetic filter' / 'mutational cleanser'. This function is served most of all by male stress mechanism in the impact on low-status (low mate-value) males. These males may benefit individually if they withdraw from competitiveness in order to bide time (until perhaps they develop in ways allowing them to compete more effectively) and to avoid further loss in status, wasted effort, and not unlikely serious injury; but, more importantly, the cortisol produced by the chronic stress of low status together with the fall in testosterone cannot but lead to a physiological fertility decline in what is auto-reproductive-suppression differentially corresponding to dominance rank [For fuller outline, see Moxon (2009, 2012)]. [Note that there is no theoretical problem here with an ostensible group-level adaptation: this is an illusory issue; a false framing. Just as dominance ranking itself evolved without any requirement for 'group selection', either naïve or as reformulated by Novak, Tarnita & Wilson (2010), so too did the associated reproductive-suppression. Selection is often misunderstood as necessarily being in terms of a multi-level conceptualisation ('individual' versus 'group'), when instead it is a matter of population genetics. A proper understanding of 'kin selection' reveals co-operation evolving through the interplay of genetic and population structuring [Lion, Jansen & Day (2011)]. Independently, Powers, Penn & Watson (2011) arrived at a similar model. An alternative perspective is that lower individual fitness in the short-term can be more than compensated by higher fitness in the long-term, through the exploitation of an aspect of the selection process itself in 'lineage selection' [Nunney (1999)]. With a number of mathematically equivalent rival models, it is more a question of which is preferred philosophically than which is empirically justified. They are complementary in addressing the same seeming paradox of selection across level, which turns out to be an artefact of how the question was posed.]

Stressing males, then, achieves several closely related ends: stress can be utilised and generated within males to drive competitiveness, with the impact of long-term stress both purging deleterious genetic material via those males who, through their low-status, suffer substantial falls in testosterone and rises in cortisol, and thereby have their potential to reproduce to some degree shut down; and the 'honest signalling' of genetic quality in those males who can gain high-status despite the impact of cortisol and testosterone. [Notwithstanding the adaptiveness of 'honest signalling', there may also be, within male stress mechanism, some physiological process circumventing the deleterious effects of long-term stress on high-rank individuals – most likely an epigenetic change of a gene concerning one of the several types or cortisol receptor — so that they are not inhibited from the potential prodigious reproduction available to them through being preferentially chosen by high-fertility females. However this is a topic on which research is hard to find.]

Though a picture of sex-specific stress mechanism has been fairly clear behaviourally for some time, the endocrinological understanding was limited, with hitherto a lack of research on the relevant neuro-hormonal pathways and in particular of the underlying genetics, to show concretely

that indeed there is a sex-dichotomy in stress response, and that it fits with the key biological principles just outlined. This impasse no longer pertains, albeit that there is still much to explore. There is now coherent multi-level general mammalian modellng of stress mechanism fully applicable to humans, as well as specifically human data.

From the foregoing discussion, what would be anticipated overall is that different stress response mechanisms from genes via hormones or directly to neural pathways are associated with females being particularly sensitive to stressors as negative stimuli, detecting them at low threshold and continuing to react against them through the above-cited greater emotional reactivity in females through lowered levels of estradiol; thereby prompting steps to alleviate the source of stress – through the oxytocin and oestrogen mediated responses in terms of the afore-discussed female 'tend and befriend' mode – and to damp down the deleterious physiological impact of cortisol aside from registering it – as seen in the afore-mentioned female inhibition of cortisol secretion by beta-endorphin, and the predominantly female binding of cortisol to ECG, rendering it inert. Males, on the other hand, would be expected to be not merely less sensitive to some types of stressor as negative stimuli, but to utilise some stressors and even endogenously to generate stress in order to sufficiently drive intra-sexual competition. This profound distinction between the sexes is evident in gross personality 'style' measures, though this has been masked by pooling of data from men and women, controlling for any sex difference, not reporting or not further investigating when one emerges, and ignoring studies where sex difference is strongly suggested or even when clear from the data. The history of neglect and wilful obstruction here, together with the evidence all too evident for anyone to find, is well set out in a review and new study [Desoto & Salinas (2015)] showing that for women, neuroticism actually correlates negatively with cortisol levels, with the correlation being positive only for men. Most simply, males would be expected to have a higher threshold for registering the impact of a stressor as stress, and to possess the facility to attenuate stress if and when it becomes chronic to the point that it is less motivational than a nuisance.

Consistent with this picture, Bangasser et al (2010) find that the receptors in the mammalian brain for corticotrophin-releasing factor (CRF) – the hormone principally responsible for orchestrating the hypothalamic-pituitary-adrenal (HPA) main stress axis, as well as directly producing autonomic, behavioural and cognitive effects – are in females both far more sensitive to low levels and unable to deal with high levels. Thus is the female driven to take steps to alleviate the source of stress and escape it. By contrast, uniquely in males there is desensitisation, as well as a much higher threshold to trigger the receptors. This sex-specificity is as a result of completely different functioning of the CRF-receptor in females (regarding the mode of signalling and compromising of receptor 'internalisation', which never occurs in males). The underlying genetic basis of this opposite CRF functioning according to sex is beginning to be revealed [Gilman et al (2015)].

Not only is the genetic – and, not least, epigenetic – underpinning of constituent pathways such as this being found, but the apex of the genetic cascade orchestrating male stress mechanism has been found to be a single key gene: tellingly, the same gene, SRY, that is responsible for male sex-determination (and known to be expressed in the brain) [Lee & Harley (2012)]. This common control is just what is found even in species far more 'primitive' than mammals; viz, the fruit fly [Argue & Neckameyer (2014)], indicating that the co-determination of stress and sex is highly conserved, phylogenetically extremely ancient, and therefore that the sex-specificality of stress mecha-

nism is a key emanation from male / female function across animal biology, with a mammalian model in all essential features encompassing humans.

It is not too much of a surprise, therefore, that a perfect sex-dichotomy – almost nil data overlap, notwithstanding unavoidable usual data 'noise' – in human acute stress response is shown in brain neuro-imaging of cerebral blood flow in consequence of mild psychological stress, irrespective of the method of analysis or classification [Wang et al (2007)]. Stress in men is here associated with increased blood flow in the right pre-frontal cortex and reduction in the left orbito-frontal cortex; a robust response persisting beyond the task. But acute stress in women activated various subcortical structures; and, unlike the male response, was poorly correlated with cortisol levels.

The progress to outline sex-specificity in stress response already is so significant that a recent summation of research included a declaration in its title that the field had undergone a "metamorphosis" [Juster & Lupien (2012)]; and this from reviewers who pointedly distinguish between sex and gender [sic], in ignorance of its being scientifically and philosophically unsupportable to maintain that any aspect of male/female could be other than at root a biological phenomenon, and revealing an ideological orientation to regard the sexes as being essentially the same. Not only do Juster & Lupien conclude that the sexes are entirely distinct, but that far from sex and gender [sic] here being antagonistic, "progress in stress research has benefited most by investigating sex and gender in synergy and not separately". They point up as a key insight that whereas women are negatively stressed by social rejection, men are "more reactive to" – in other words, they are driven by – achievement-based stressors. This major divide is also what is found in a review of psychosocial stress in adolescence [Sordaz & Luna (2012)]. Study of reward-seeking reveals that stress motivates men in this regard, yet women shy away; the sex-specific underlying brain activation patterns being identifiable from functional magnetic resonance imaging (fMRI). Neural activation in the dorsal striatum and anterior insula (areas of the forebrain closely connected with the amygdala, which is located below and is evolutionarily more ancient than the cerebral cortex) increases in men but decreases in women – an opposite mechanism according to sex [Lighthall et al (2012)]. This is in line with previous work by Lighthall and collaborators, and by others, as Lighthall reviews; directly connecting stress with competitiveness.

Studies of the impact of chronic stress – which is more interesting and revealing of principal patterns than mere acute stress — have been reviewed, with a focus on limbic (mid-brain) structures; first by McLaughlin, Baran & Conrad (2009), who concluded that the profound changes entailed are mostly restricted to males, with what effects do appear in females being opposite. For males, there is substantial retraction of nerve cell dendrites in the hippocampus and, conversely, hypertrophy (dendritic extension and proliferation) in the amygdala; neither of which occurs in females: and although for males there is further dendritic retraction in the prefrontal cortex, the opposite is the case for females. These very different patterns create a considerable imbalance between the component limbic structures in males but not in females, resulting in markedly less behavioural flexibility and greater emotional and motivational arousal for males; whereas, in respect of both of these effects, the inverse though less pronounced changes for females. The amygdala is the structure where basic drives, emotions and memory are integrated in motivation, and it is telling that it is only in this mid-brain region in males where innervation is developing as a result of prolonged stress – consonant with the afore-cited work by Lighthall on reward-seeking and brain areas closely connected to the

amygdala. The prefrontal cortex would bring higher functions to bear, but with the retreat in innervation in the male, then there is prevention of too much cognition getting in the way of the amygdala's work in utilising stress to drive intra-sexual competitiveness. Similarly, the hippocampus would link-in very basic homeostatic maintenance activity in the evolutionarily most ancient parts of the brain – the brainstem and associated structures; but, here again, in the male the neural shrinkage indicates an overriding of such interference in managing long-term stress.

The most comprehensive and detailed investigation cum review in the literature of chronic stress (and also acute stress, but this is here ignored in the context to avoid confusion and because the findings are more complex and equivocal), setting out in great detail highly complex inter-related systems at several levels [Sterrenburg (2012), incorporating Kozicz, Sterrenburg & Xu (2011) and Sterrenburg et al (2011, 2012)], ends likewise in a conclusion that major limbic changes in the male are not apparent in the female; going further in stating that the limbic regions are activated only in males, and that there is a plethora of further profound sex-specificities, in what is a very large piece of work beyond the scope of the present review to summarise more than in a near cursory manner. The key conclusions relevant to the present paper are that only in males is neuronal CRF messenger RNA increased in the paraventricular nucleus of the hypothalamus – the inverse of the sex-dichotomy when the stress is merely acute: then, only in the female is the very same change — with other immediate early gene expression apparent in several key limbic regions; whilst CRF in females actually declined. This replicates previous findings [Duncko et al (2001)] and indicates that males synthesise replacement CRF to match what has been released, though females simply use up existing CRF and don't replace it. The male overall response, then, is not simply active rather than passive, but is amplified; the inverse of the female pattern of generally a passive response, which would work well for females as a default strategy to escape the sort of stressors females typically encounter. Strikingly, below the level of neuro-hormonal pathways, Sterrenburg identifies sex-specific epigenetic changes: altered degrees of transcription of the CRF gene — here by all the four modes, of DNA methylation/ demethylation and histone acetylation/ deacetylation – in different key parts of the limbic system, including the amygdala and the paraventricular nucleus of the hypothalamus. These epigenetic changes in one sex are against an opposite or null change in the other. Other important sex-specificities include a male-only increase in the messenger RNA of the neuropeptide, urocortin, in the midbrain centrally projecting Edinger-Westphal nucleus [Derks et al (2010)], which is found to be strongly elevated in male but not female suicides [Kozicz et al (2008b)].

Sterrenburg's research programme cum review for all its detail and depth points up how much work remains to be done in unravelling and integrating the inter-related pathways and genetic/ epigenetic/ neuronal/ hormonal levels in stress mechanism, to construct models where the multiple component axes, systems and levels coordinate. This is dauntingly complex given additional related systems coming under investigation as it is realised they are part of stress mechanism, and which also display sex-specificity; such as the major mode of neuro-transmission within limbic structures by glucomates, which are modified in various ways in both acute and chronic stress scenarios by cortisol. Several of the glucomate amino acids utilised as neurotransmitters and their various receptors act in different parts of these brain regions (the hippocampus, the prefrontal cortex and the amygdala) in sex-specific ways to impact on memory and cognition [Wang et al (2015)]. Another example is the impact of serotonin on the HPA axis [Goel & Bale (2010)], whereby greater expression of serotonin receptors in the pituitary gland boosts female stress responsiveness. Nevertheless, the progress

made in the past few years has been rapid and surprisingly detailed, with already complex modelling all the way down to individual gene base-pair epigenetic changes, far ahead of the former vanguard of tenuous, rough and highly qualified outlines typically from assays of cortisol and one other hormone in the investigation of their co-variation under stress.

Everywhere investigators probe, sex-specificity is easily found, reinforcing its paradigmatic force. More focus is required on distinguishing sex-specificity according to a dimension additional to sex and type of stress: type of stressor. Already noted is the major distinction between social relationship and achievement being key stressors respectively for women and men; which would be fully anticipated from the foregoing discussion of the nature of stress according to sex. Other stressors may not be so obvious as to their likely or possible sex-specificity. Within both acute and chronic stress scenarios, there are stressors pertaining to only one sex or the other. As well as for early acute social stress of isolation, it is now known that early chronic isolation stress has profound sex-specific long-term impact on males [Eg, Elfwing et al (2015)]; and also that restraint produces greater cortisol reactivity in females [Turner et al (2010), Babb et al (2013)]. There are a number of other recent studies regarding both acute and chronic stressor/sex interaction across phyla (from insect models through fish to mammals) [eg, Anthenelli et al (2014), Freitak et al (2012), Donaldson et al (2014), Sanders, Stevens & Boeh (2010)], but they are usually confined to some component of mechanism, leaving conclusions heavily qualified because of the highly complex interaction of multiple systems in stress response. To make matters worse, some stress protocols within experiments may so poorly reflect stress as usually experienced in the natural environment as to have little value – an absence of external or ecological validity. Consequently, stressor-specificity is a sub-topic where comparability across studies is very limited, with no review to make overall sense of how stressor type interacts with sex as yet attempted (and, certainly, such would be beyond the scope of the present review). This is surely soon forthcoming, however; given that the additional factor of stressor type can provide a key to further unlock the nature and basis of stress sex-specificity. On the other hand, a three-way matrix of sex, type of stress and type of stressor, in being such an obstacle to comparability provides great scope for confusion in the literature and an open door to the ideologically hidebound to avoid experimental design where sex-specificity is detectable, let alone to test it as an hypothesis. It is indicative of the profundity of the sex-specificity being revealed, that far from being obscured by inter-relating factors as yet not fully explored, instead it has become so fully recognised as to become the new paradigm in research.

The sex-specificity of stress mechanism has major implications for other aspects of animal and human biology in prompting a corresponding sex-dichotomous approach as it is realised that this generally has been long neglected. The most obvious study area here would be mechanism underlying the epiphenomenon of dominance hierarchy, which, long having been recognised as quintessentially male sociality, clearly relates to stress mechanism in that it likewise concerns male intra-sexual competitiveness and, necessarily in turn, the root male function of 'genetic filter' / 'mutational cleanser'; and now is shown to be underpinned by the SRY gene, confirming its male-specificity [Van den Berg, Lamballais & Kushner (2015)]. Van den Berg, Lamballais & Kushner have discovered that whereas males require and make use of past experience of contests with all same-sex others in the group to bias their future efforts to either properly contest or back off, females always engage anew at each meeting (even with those previously encountered), simply by assessing the other in terms of their apparent inherent attributes. Both of these sex-specific modes produce

ostensible same-sex transitive hierarchies, but the female apparent hierarchy is not transitive and has no social reality; it's artefactual. Only males possess the neural mechanism to process either 'winner' and/or 'loser' effects necessary to produce an actual hierarchy. The same research team is soon to publish a study directly examining 'winner'/'loser' effects, and preliminary results indicate a fundamentally different proclivity to process and integrate social experience, confirming the male-specificity of actual rather than artefactual dominance hierarchy.

This important new direction in understanding the nature of dominance hierarchy is an example of how the new paradigm of sex-specificity widening out from the study of stress mechanism, with investigation right down to genetic and epigenetic levels, can bridge between biological theory and observable behaviour and inferred cognition to significantly contribute to an integrated, cross-level understanding of the 'symbiotic' very different functions of the sexes.

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