

How asymmetrical before it is asymmetrical?

Thou hast no faults, or I no faults can spy;
Thou art all beauty, or all blindness I.

Christopher Codrington

The last ten years have witnessed the shifting fortunes of the fluctuating asymmetry (FA) paradigm (called the “fluctuating” paradigm by Simmons *et al* 1998). FA is the small (often < 1%) random deviations from perfect bilateral symmetry that occur during the development of symmetrical traits. The asymmetry is considered to be indicative of developmental instability or the inability of the genome to buffer development against environmental stressors (Swaddle 1999). It is supposed to provide a reliable indicator of genetic quality (Møller and Pomiankowski 1993). The role of FA in sexual selection was first suggested by Møller (1990). Since then an explosion of studies on the effects of FA on mate choice has occurred in organisms ranging from earwigs, to birds, deer and humans (reviewed in Møller and Thornhill 1998). This paradigm has come under attack for a variety of reasons which is perhaps expected whenever a new paradigm is proposed (Simmons *et al* 1998). Criticisms range from the repeatability of estimations of developmental stability using FA (Van Dongen 1998), the FA effect as a statistical artifact (Nachman and Heller 1999), publication bias (Palmer 1999), and also whether development stability as measured by FA and fitness are really negatively related (Clarke 1998). These criticisms should serve to make researchers in this area more circumspect, and should certainly improve the quality of the research designs.

Two additional criticisms that deal with the nature of the asymmetry as a biological signal are important because these criticisms attack the very basis of the fluctuating paradigm. One problem concerns dissecting out the true signalling properties of asymmetry independent of other confounding parameters, e.g. if experimental manipulations of symmetry also influence other factors such as flight performance in the asymmetrical tail feathers of swallows, then alterations in behaviour caused by the asymmetrical trait may be the actual biological signal and not the asymmetry itself (Swaddle 1999). This is relevant for morphological traits but may not be so relevant for sexual ornamentation such as chest bars on male zebra finches or vertical bars in sailfin mollies which are believed to influence female choice. The other and possibly more serious problem is that very few experimental studies have used asymmetry values that represent the asymmetry actually found in natural systems (Swaddle 1999). This exaggeration of asymmetry in experimental manipulations, e.g. 10% asymmetry in chest plumage of male zebra finches and 21% asymmetry in bar patterns of male swordtail fish (Swaddle and Cuthill 1994; Morris and Casey 1998), can have very serious consequences for the interpretation of the relevance of the natural biological signal.

Another major concern with studies aimed at finding a connection between FA and mate choice, is whether the experimental subjects can actually detect natural levels of asymmetry independent of other cues. The first study to examine this is an investigation of the threshold for detection and behavioural response to length symmetry in the European starling *Sturnus vulgaris* (Swaddle 1999). Using an operant conditioning system, Swaddle projected paired symmetric and asymmetric vertical bar images (black on a light background) simultaneously onto pecking keys. Half the birds were trained to peck at the symmetric keys for a reward, the other half were rewarded by pecking at the asymmetric keys. Asymmetry values of 10%, 5%, 2·5%, 1·8% and 1·25% were used, and it was found that birds were able to detect an asymmetry of 1·8% and above but not of 1·25%. There was no difference in the response between birds trained to peck at asymmetric or symmetric keys thus refuting the suggestion that the subjects found it easier to learn associations with asymmetric rather than symmetric objects. In each trial using a different asymmetry level, Swaddle presented 20 pairs of symmetric and asymmetric bars in which the overall mean bar size ranged from 0·5 cm to 2·0 cm in gradations of approximately 0·08 cm resulting in 20 bar lengths in each set of symmetric and asymmetric images. Each member of the pair of symmetrical and asymmetrical images was randomly picked from this set of 40 images for a particular asymmetry level. Swaddle was therefore able to separate length from asymmetry by using these random selections. Furthermore, Swaddle presented the asymmetry treatments in the following order:

10%, 5%, 2.5% and 1.25%. On finding that there was a sharp drop in the proportion of correct responses at 1.25%, Swaddle reasoned that it was possible that the birds were merely habituating to the presentation of stimuli and were no longer responding to perceptible asymmetry differences. He, therefore, immediately exposed the same birds to a new set of 10% asymmetric stimuli, and found that the symmetry detection immediately returned. Swaddle then continued with a set at 1.8% asymmetry differences, and found that the asymmetry detection was nearly the same as at the 10% difference. He was therefore able to conclude that the threshold detection capability was somewhere between 1.25 and 1.8%. This finding corresponded well with earlier studies on the visual acuity of pigeons (Macko and Hodos 1985), possibly indicating general thresholds for the avian visual system. Swaddle cautions that his studies need to be refined using other types of visual patterns, such as random dot patterns and shape differences rather than vertical bar presentations, as it is possible that in the paired bars, the birds were responding to rectangular (paired symmetric bar patterns) versus irregular topologies (paired asymmetric bar patterns).

Swaddle's study is valuable because of the caveats that it generates. We need to know more about the perceptual systems of organisms before we infer connections between a signal and its evolution by sexual selection. Additionally the heritabilities of secondary sexual characters need to be investigated as also their links with developmental stability and reproductive success. According to Simmons *et al* (1998), the proportion of studies supporting a role of FA in sexual symmetry has declined steadily from 100% in the early part of the last decade to a current value of about 36%. These authors claim that this is because of an increasing improvement in methodologies and an increasing tightening up of experimental design. The "fluctuating paradigm" may come to rest at a stable point soon or may be completely discarded; it is early days yet.

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Stress, depression and hippocampal damage

Stress is part and parcel of the daily interaction between an organism and its environment. Most responses to stressful environments are adaptive and allow an animal to reestablish its homeostatic balance. It is the maladaptive responses to stress that are thought to be relevant in the precipitation and exacerbation of psychiatric disorders like depression and post-traumatic stress disorder (PTSD) (Sapolsky 1996).

Amongst the prime targets of stress in the brain is the hippocampus, which has high receptor levels for corticosteroids that are released during stress (McEwen 1999). Over the years evidence has built up that stress leads to damage of the hippocampus. Initial reports from Uno *et al* (1989) indicated that primates exposed to psychosocial stress in the wild had considerable hippocampal neuronal loss. Laboratory experiments then clarified that stress exerts diverse effects on different hippocampal subfields (McEwen 1999). Chronic stress causes atrophy and eventually may lead to the death of hippocampal CA3 neurons. In addition, stress also suppresses ongoing adult neurogenesis in the hippocampal dentate gyrus (DG) subfield. Unlike most regions of the brain where neuronal proliferation is restricted to discrete stages of development, the DG retains the ability to exhibit neurogenesis throughout adulthood in several species, including rodents, primates and humans (Kempermann and Gage 1998). The influence of stress on neurogenesis and neuronal atrophy/death are likely parts of a cascade of events that eventually results in stress-induced hippocampal damage. Hippocampal damage is thought to play an important role in the etiology of stress-related psychiatric disorders, and decreases in hippocampal volume have been observed in patients of recurrent, major depression and PTSD (Brown *et al* 1999).

Depressive disorders have often been associated with high levels of circulating corticosteroids. Several brain regions including the hippocampus mediate central control of the hypothalamo-pituitary-adrenocortical (HPA) axis which regulates secretion of the stress responsive corticosteroids. The hippocampus is known to provide an inhibitory feedback to the HPA axis. Hippocampal damage then would result in disinhibition of the HPA axis and excessive circulating corticosteroids, which in turn are known to cause further hippocampal damage, thus setting in motion a self-perpetuating vicious cycle (Fuchs and Flugge 1998). In addition to a reduction in hippocampal volume, a decreased feedback control of the HPA axis has also been observed in patients of major depression.

The mechanisms underlying the damaging influences of stress are as yet unclear, although a number of factors have

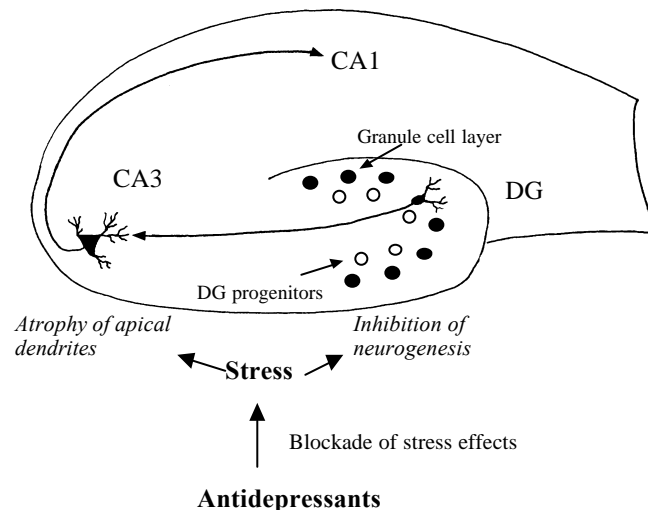


Figure 1. Schematic diagram of the hippocampus and the influence of stress and antidepressant treatments on the hippocampal subfields. The CA1, CA3 and DG comprise the main hippocampal anatomical subfields. The granule cells within the DG project via the mossy fibre pathway onto CA3 pyramidal neurons, which in turn send Schaffer collaterals that make synapses on CA1 pyramidal neurons. Exposure to stressful stimuli leads to CA3 dendritic atrophy and neuronal loss and a suppression of ongoing neurogenesis in the DG. Certain antidepressant treatments have been shown to block stress-induced CA3 dendritic atrophy and enhance DG neurogenesis.

been implicated. Activation of glutamatergic and serotonergic neurotransmitter pathways, disturbed calcium homeostasis, increased corticosteroid levels and altered growth factor expression are amongst the chain of events that are set into motion by stress. Glutamate, serotonin and corticosteroids all exert powerful influences on CA3 atrophy and DG neurogenesis. There is evidence to show that this atrophy is reversible and one can envisage that ongoing hippocampal neurogenesis is also likely to recover on adaptation to stress. There are likely several checks and balances on the path to stress-induced hippocampal damage. The question that arises then is what leads to the breakdown of these checks and balances and can one reinstate them?

The possibility that hippocampal damage may be reversible suggests that reversal of the stress-induced damage may be a potential therapeutic target for antidepressant treatments. The therapeutic action of these treatments is dependent on chronic administration for several weeks suggesting that it is a long term adaptation that underlies their therapeutic efficacy. It is possible that one potential target for antidepressant treatments is the blockade and reversal of stress effects in the different hippocampal subfields, as well as positive influences on hippocampal structural plasticity. Indeed, certain antidepressants prevent the stress-induced CA3 dendritic atrophy. We have recently shown that electroconvulsive seizure administration, which is clinically used as a potent antidepressant treatment, increases the sprouting of the mossy fiber pathway of hippocampal granule cell neurons (Duman and Vaidya 1988). In addition, recent data indicate that chronic antidepressant treatments enhance the proliferation of neuronal progenitor cells within the DG of the hippocampus (Duman *et al* 1999).

Overall accumulating evidence suggests that hippocampal structural plasticity may be a critical component of both adaptive and maladaptive stress responses, and in addition may also be a component of the therapeutic adaptations following chronic antidepressant treatment.

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