

PART II

Themes



Aggression: towards an integration of gene, brain and behaviour

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Overview

Aggression ranks among the most misunderstood concepts in the behavioural sciences. Commonly viewed as an aberrant form of behaviour, situations of conflict are pictured in the context of unfavourable or stressful circumstances, brought about by amoral urges, in critical need of our cognitive control, and with negative consequences for all involved. Such a view fundamentally misunderstands the biological significance of all behaviours that occur in the context of attack, defence or threat. Deeply rooted in the demands of the natural world, the ability to assert oneself represents a critical solution to any individual's need for self-preservation, defence of its interests or resource competition. Examples of aggression are found throughout the entire animal kingdom, regardless of its bearer's specific neural or cognitive faculties, phylogenetic origins or sociobiological circumstances. It has become abundantly clear that aggressive traits have been shaped by evolution like any other behavioural phenotypes, and a range of underlying mechanisms in the causation of aggression are now being unravelled.

This chapter aims to present a comprehensive overview of the issues that are encountered when

trying to understand the *hows* and *whys* as individuals oppose each other. The chapter focuses special attention on delineating distinct behavioural phenomena such as aggressive tendencies, dominance or violence. Game-theoretical considerations offer a powerful theoretical framework to assess the evolutionary consequences of different behavioural strategies. A discussion of proximate mechanisms attempts to link these behavioural heterogeneities to the functioning of underlying neural and endocrine control systems. Three case studies review powerful interdisciplinary approaches, which uniquely bridge multiple levels of organisation. First, the application of recombinant DNA technologies and behavioural genetics to the aggressive behaviour of fruit flies *Drosophila* spp. has produced novel insights into the behaviour's essential brain circuitry. This approach may allow us to image the functional roles of embedded neurons in living animals as these respond to behaviourally meaningful cues. Second, recent evidence, linking violence or lack of impulse control to amine metabolism in primates, illustrates the social and endocrine conditions in which aggression and fierce behaviours may be appropriate and selected

for. Third, efforts to select for enhanced levels of aggression in distinct genetic strains in dogs and mice generally produce, within a few generations, animals with levels of aggressive behaviour that

greatly exceed those of controls. This chapter thus aims to integrate a diverse range of approaches into a better understanding of aggression, its functional roles, and its neural and hormonal causes.

7.1 Introduction

Aside from sex, few animal acts match aggression's ability to attract and hold our attention. Actions during conflict feature some of the most spectacular and dramatic behaviours of a species' repertoire. Imagine two northern elephant seal *Mirounga angustirostris* bulls locked in mortal combat on a deserted, rocky, windswept beach, copious amounts of blood flowing into the churned-up sea, with a harem of on-looking females desperate to escape the mayhem developing around them. Although cases of such unbridled social hostility are relatively rare, the basic tendency towards aggression appears almost ubiquitous. Aside from aggression's general prevalence, fundamental rules governing combat seem to be just as natural and widespread. In most species, aggression relies mostly on highly visual and elaborately ritualised displays, which effectively channel aggression, govern the conflict's resolution, and structure how individuals interact (Lorenz 1963, Archer 1988, Nelson 2005).

As we witness animals engaged in situations of conflict, we cannot help but be drawn in by the behaviour's inherent relevance to our own biological roots. Demanding attention from generations of behavioural scientists across a wide range of disciplines, interests include proximate, neural or endocrine causes of aggression, alongside the role social roots play in its expression. We explore the eye-catching behaviours that make up social encounters, analyse the effectiveness of different strategies, advance powerful predictors that eventually help settle them, and assess the social consequences that emerge in their wake.

7.2 Evolutionary perspectives

Conflicts are energetically costly and inherently carry a wide range of risks. Natural selection offers

a powerful conceptual tool, as it is expected to refine behavioural decisions and strategies so that they maximise beneficial outcomes for each individual involved (see Chapter 6). The meeting of two clawed crustaceans, for example the American lobster *Homarus americanus* or its crayfish cousins, matched in size and willing to do battle, epitomises a typical scenario for highly structured fighting (Huber & Kravitz 1995). Opponents engage in a sequence of hostilities where intensity increases in discrete steps as long as the fight lasts. Serving to illustrate constituent concepts of aggression and how these may relate to one another, the encounter begins as one individual approaches another intent on attack (Fig. 7.1). The threatened crustacean, depending on its own aggressive state, may respond in kind. Combatants advance towards each other with vigorous whips of the antennae that signal readiness to step up the encounter to the next intensity. In an escalating sequence of behaviours, opponents first touch with wide-open claws, grab and hold in attempts to displace each other with pushes, pulls and lifts, and finally resort to unrestrained use of their weapons. During such escalating encounters, combatants are able to assess each other's relative abilities and strengths in a stepwise fashion. Despite the presence of potentially lethal weapons in many taxa, their use is largely restricted to fights among closely matched opponents, where a series of earlier stages had failed to yield a clear winner (Hofmann & Schildberger 2001).

7.2.1 Aggressive state

Not all individuals are equally likely to engage an opponent, and intensities vary greatly from a restrained, delicate threat display to fierce, unbridled charges. Such individual differences in attack tendencies are ascribed to an animal's aggressiveness or aggressive state. As in other forms of arousal and



Figure 7.1. Fighting crayfish *Astacus astacus*. Photo: Robert Huber.

motivation, this term is used purely as an intervening variable (i.e. a hypothetical, helpful construct), which justifies its use only in those instances in which it effectively simplifies our understanding of the observed behavioural phenotypes. It makes no claims, however, to accurately represent the true number and nature of internal factors that feed into it. We must acknowledge that if we had a truly comprehensive understanding of how an aggressive behaviour was produced, we would have no need for this term at all. Contingent on social conditioning and past events, and influenced by a variety of neural, endocrine and genetic factors, aggressive state represents a top-down effort to operationally characterise behavioural variation until we can offer a better understanding of its actual causation. Despite these limitations, concepts of motivation help us to understand which brain systems mediate the psychological processes that guide real behaviour (Berridge 2004).

7.2.2 Fight strategies

In most scenarios, ritualised displays take the place of unchecked, aggressive interactions, as all-out fighting between members of a species is rarely in

anyone's long-term interest. Game theory provides a powerful and formal understanding of why animals only tend to fight with great ferocity when a resource of exceptional value is at stake (see Chapter 4; Dugatkin & Reeve 2000). The Hawk-Dove game explores conditions that optimise the beneficial consequences during resource-centred conflicts (Maynard-Smith 1982). The behavioural strategy of a Hawk is to readily use its weapons during the fight until either it sustains an injury or its opponent retreats. A Dove, in contrast, contests the interaction with displays only. If faced with a Hawk, a Dove will retreat immediately as the opponent threatens to use its weapons. A formal payoff matrix shows the different players' consequences for all possible combinations of strategies (see Chapter 4), where each individual would prefer to win, prefer to tie rather than lose, and prefer to lose rather than receive injury. In encounters between Hawks, the winner gains control over the value of the resource while the losing Hawk sustains an injury. Expectations from this model demonstrate that in situations where the cost of injury exceeds the benefit of winning, populations are expected to adjust to balanced proportions of the two strategies – the great majority of individuals will fight in highly restrained fashion, while a

small number of Hawks persists. In rare cases where the value of an exceptional resource exceeds the cost of injury, a Hawk strategy will be widespread as it always carries an advantage over Doves, replacing the latter completely. Fighting, for instance, is particularly intense in elephant seals, because in this case a victorious male monopolises a section of the shore, along with sole reproductive access to a group of females who reside on that part of the beach. In the great majority of instances, however, resources are rarely worth the risk of being injured, and competing individuals will do best by resolving conflicts with ritualised displays only (see Chapter 4; Maynard-Smith 1974).

Additional strategies for signalling and assessment in fighting exist within War of Attrition scenarios (Maynard-Smith 1982). As fighting slowly progresses through levels of increasing intensity, both individuals gain detailed, cheat-proof information about their opponent, while they grind down the opponent's defences by inflicting continued small damages. There is no fixed cost associated with losing or contesting but, as the encounter wears on, each player accumulates incremental costs. When an individual decides to back down, it effectively relinquishes access to the contested resource, rather than continue to sustain further insults. The emergence of structured fighting behaviour thus clearly represents a favourable option for all parties, and has given rise to the evolution of encounters that are conducted with a stepwise comparison of signals.

Skill in assessing the relative strength of an opponent is key for navigating the demands, risks and opportunities of social living. Selection will favour those with an ability to effectively anticipate their chances well in advance, and to choose the most beneficial strategies. When an animal is bested by an opponent, it is always far better to adopt submissive behaviour and accept subordinate status, rather than risk something far worse. Decisions to retreat come suddenly and often without warning, as a combatant begins to regard its chances of winning as increasingly slim. Game theory also confirms that opponents should only signal strength while hiding any intentions to eventually withdraw

(Maynard Smith 1974, Számadó 2008). A wide range of attributes decides between victory and defeat. In invertebrates, where individuals generally pursue a solitary existence, physical superiority is often the primary determinant of an interaction's eventual outcome. With prominent asymmetries in the size of body or weapons, or in sex or reproductive status, most fights are resolved quickly. In vertebrates, aggressive success depends to a great extent on the ability to form successful alliances, to harness cognitive skills, or to inherit status from high-ranking kin. In addition to size and strength, success is contingent on the development of social competence (Suomi 1997).

Natural selection enhances overall effectiveness in aggression, rather than absolute amounts of it. High-ranking individuals will most likely display a favourable combination of strength along with ability to titrate their levels of aggression, to pick fights that are winnable, and to compete only in those that are worth it. Hyper-aggression (see Chapter 14) describes behaviours that appear to greatly exceed the most effective norm – individuals who readily launch the initial attack even in situations where they ought not to, who are overly eager to escalate or retaliate, who show a willingness to follow an excessively physical trajectory even when an opponent has already withdrawn, or who fail to back down in situations where there is little prospect of winning. Such behaviours rarely make for an effective strategy, as they coincide with greater risk of injury or death, or, in the best-case scenario, gaining a low rank.

7.2.3 Dominance

When winning one or more prior encounters produces a lasting polarity in the outcome of future bouts between a given pair of individuals, a dominance relationship has been established (see Chapter 14). In its most common form, the past loser will be less likely to initiate further bouts against the winner, or will retreat quickly if confronted (Chase *et al.* 1994). Most instances of dominance rely on individual recognition or familiarity, which establishes learned, pair-wise relationships. Alternatively,

the recognition of an opponent's aggressive state, or of signals that indicate past success, may serve similar roles. Memories of past social encounters also impact future behaviour regardless of the opponent. These are collectively grouped into winner/loser effects, and recent winners often become likely to win again even when faced with a novel opponent, while general chances for success further decline in former losers (see Chapter 14; Dugatkin 1997). Such effects rarely impact actual fighting abilities, but rather seem to alter an animal's aggressive state or self-assessment of future outcomes. In general, the relative magnitude of loser effects often exceeds those of winner effects and is frequently longer-lasting (Chase *et al.* 1994). Moreover, loser effects by themselves are often sufficient for maintaining stable hierarchical relationships and social structure (Hock & Huber 2006). Empirical evidence for the existence of winner and loser effects derives from a wide range of taxa, yet the mechanisms that underlie them are still poorly understood (Hsu & Wolf 2000). Current evidence suggests that proximate causes for winner and loser effects reside in behavioural-neuroendocrine feedback loops for aggression (see below and Chapter 17).

As individuals repeatedly meet and interact with others, higher-order social organisation emerges through a series of sequential dyadic interactions among the group members. Individuals of many species, including humans, tend to arrange themselves in linear social hierarchies (Wilson 1975, Hemelrijk 1999). Although relatively fixed individual characteristics such as size, strength or agility often determine their owner's rank, these characteristics are more often overshadowed by contextual factors and chance events (Chase *et al.* 2002). Experiments in which identical groups are repeatedly reconstituted result in similar overall hierarchical structures, although individuals show surprising variation in the final ranks they occupy (Chase *et al.* 2002). Moreover, the ranks that individuals establish is highly dependent on the order in which they join the group. Prior residence effects confers significant advantages to those members who establish themselves early (Huntingford & Garcia de Leaniz 1997). With future

success contingent on past interaction histories through social conditioning, the emergence of social rank is critically governed by a host of dynamic, self-structuring properties. The importance of self-assembly in structuring a web of dominance relationships within the group is supported by a host of empirical evidence (Theraulaz *et al.* 1995, Bonabeau *et al.* 1997, Goessmann *et al.* 2000, Beacham 2003). Theoretical models explore the outcome of situations in which initially similar entities perform a series of self-reinforcing dominance interactions (Dugatkin & Dugatkin 2007). Ranks differentiate as individuals lose to an opponent early and are consequently slated for lower ranks than those who won during the critical, initial stages. The stability and precise structure of hierarchies thus represent an automatic consequence of the progressive polarisation in dominance status (Hock & Huber 2006). As some individuals become multiple losers, their aggressiveness further declines along with any opportunities to engineer future rank reversals. Ranks may be evenly spaced, or biased towards a few very dominant or subordinate individuals. The self-reinforcing effects of winning and losing may also extend to bystanders, where unrelated third individuals automatically either submit to a winner or dominate a loser (Grosenick & Fernald 2007).

7.2.4 Human aggression

Human ingenuity for inflicting intentional harm is without equal, although warring tendencies may already be rooted in a deep, pre-human past (see Chapter 15; Wrangham & Peterson 1996). Instances of violence have been documented for a range of non-human apes and may arguably have been wired into our genes when aggressive ancestors shoved the nice guys aside, seized the females, and reproduced. Humans, however, with their searing capacity for cruelty, killing, torture and rape, are clearly in a category of their own when basic, violent tendencies combine with a burning intellect that excels at harnessing novel techniques and implements. Aside from an unprecedented potential for carnage and destruction, we are at the same time also capable

of the most remarkable instances of compassion, understanding and peaceful negotiation. The direction depends on each individual's ethical codes and moral norms, driven by societal expectations, good parenting or social contexts (Pinker 2007). A clear vision has emerged where 'natural' tendencies for aggression appear to be ubiquitous, but so too are a plethora of sophisticated mechanisms that keep conflicts in check, channel aggression, negotiate fighting signals, resolve conflicts, and ultimately govern social group structure.

7.3 Definitions, misconceptions and solutions

It is quite remarkable that, despite this wealth of empirical and theoretical attention, a comprehensive synthesis of aggression and of its biological roots has stubbornly remained elusive. A central explanation for this paradox resides in the lack of a unified, operational definition of aggression across disciplines, and of a general agreement on what the term actually includes. For instance, psychologists define aggression as 'all behaviour that is intended to cause bodily harm' (Krahé 2001). Moyer's (1968) widely adopted classification of aggression recognises multiple subtypes, including competition between males, a mother's efforts to protect her offspring, and fighting as a learned response to cope with a particular situation. Biologists regard a definition that focuses solely on injury as inadequate, because it excludes a wide range of threat behaviours directed at rivals – birds that challenge their adversaries with song, an impala's exaggerated strutting as a signal of strength, or a resident's territorial claims through scent markings. Moreover, there is little agreement on whether a predator's hunting behaviour is included – a lion chasing and killing a gazelle undoubtedly inflicts injury, but it is debatable whether this represents aggression any more than a cow cropping the top off a clump of grass. Efforts to define animal aggression with a broader focus on all behaviours of attack, defence and threat have proven considerably more practical (Immelmann & Beer 1992).

Disagreements on terminology combine with common misconceptions that treat aggression as a single, unitary concept. The latter, either explicitly or tacitly, views different study approaches simply as separate perspectives on the same underlying phenomenon. Many concepts seem so intimately related that we are tempted to view them with much overlap or even synonymously, including the occurrence of fighting, effectiveness in a contest, or an ability to socially dominate others (Francis 1988). A more compelling view acknowledges aggression's multidimensional nature and uses the term simply as an overarching term for an entangled complex of multiple, distinct components, causes and functions. Behaviour during aggressive encounters always involves the relative strengths of contrasting impulses for attack with a tendency to flee – rarely is either present entirely alone. To acknowledge a difficulty of separating these components, the term *agonistic behaviour* has been introduced. The term specifically addresses the balance of forces for both attacking and fleeing, and it accommodates all instances of attack, threat or defence (i.e. offensive agonistic behaviour) alongside escape and submission (i.e. defensive agonistic behaviour). The most comprehensive and practical definition of aggression has arguably emerged from an evolutionary viewpoint (Alcock 2005). In this context, aggression includes all behaviour directed at increasing an attacker's reproductive prospects at the expense of the attacked or threatened rival. Interspecific contests also focus to a greater extent on competitive interactions, rather than on predator-prey scenarios.

Attempts to search for proximate mechanisms underlying aggression critically require us to characterise aggression's natural building blocks, to recognise the various factors that control them, and to effectively label their behavioural expression in the form of consistent and reliable behavioural phenotypes. A quantitative characterisation of agonistic behaviour usually commences with a compiled list of behaviours and analyses that report observed frequencies, rates and durations. Unfortunately, measures of behaviour that focus on *'what'* an animal

does are intrinsically sensitive to the variability inherent in behavioural systems. A focus on 'how' individuals conduct their fighting examines the higher-order structure present within behavioural frameworks and offers a substantially better alternative than descriptions of any particular instance. It thereby centres on behaviour as a series of structured rules which remain largely constant across a wide range of scenarios. Estimates for the rate at which opponents escalate the encounter are surprisingly stable even across fights that vary widely in the particular behaviour patterns used, the duration of the encounters, or the intensity with which combatants conduct themselves (Huber *et al.* 2002). Reliance on the encounter's structural characteristics assesses behaviour in the form of particular fighting strategies rather than accounting for activity on a minute-to-minute basis. Structural features are used to provide estimates for an individual's intrinsic aggressive tendencies, to identify their particular attack strategies, and to determine the rules that govern decisions for escalation and retreat (Chen *et al.* 2002).

A willingness to submit to an opponent may also depend on the perceived value of the resource at stake (Dugatkin & Dugatkin 2007). With significant prior investments in it, a mother will be likely to defend her young even when faced with a superior foe, a resident may not be willing to give up a shelter containing its food stores without a fight, or a male with reproductive access to a harem of mates may not relinquish it easily. As such instances make for striking observations, these different situations are frequently regarded as distinct, fundamental subtypes of aggression. Although this view may be tempting, shared fundamental scenarios in which knowledge about the salient value of a resource constrains the available options may not, in fact, warrant this. Moreover, instances of unusually heightened aggressive state show considerable, but poorly defined, overlap with similar higher-order concepts, including impulsivity, risk-taking, lack of behavioural control, violence, or detrimental consequences of stress (Dugatkin & Dugatkin 2007).

7.4 Case studies

7.4.1 The fruit fly fight club

Model behavioural systems have been widely used for the study of aggression. These allow detailed examination of the behaviour, addressing essentially all the features highlighted above, but now being performed in artificial settings designed to simulate real-world situations. They offer additional great advantages, however, in being able to control the rearing, handling and social experience of animals from conception, and in the ability to subsequently ask what is happening in the nervous system underlying the behaviour. An ideal organism for exploring the roots of aggression would allow precise examination of the genetic, environmental and hormonal factors contributing to the aggressiveness of individual animals. The animals should be willing to compete over desired resources in an experimental arena with sufficient ethological constraints built in to allow any results obtained to be related to real-world situations. Ultimately one might want to map the brain circuitry essential to the behaviour, and possibly image the involved neurons while they function in living animals responding to behaviourally meaningful cues. Finding a single experimental model that will satisfy all these criteria is a tall order for most of the models that have been used thus far in the study of aggression. One recently developed model using fruit flies, however, comes close to meeting these demands.

Historical background

It was not well known until recently that common strains of male and female fruit flies show agonistic behaviour in same-sex pairings. This despite the fact that aggression between male fruit flies had been described in the larger Hawaiian species (Spieth 1968, 1974, Boake *et al.* 1998) as well as in a much earlier paper on sexual selection (Sturtevant 1915). In addressing situations in which two males are courting the same female, Sturtevant wrote: 'In such cases they [males] may sometimes be seen to spread

their wings, run at each other, and apparently butt heads. One of them soon gives up and runs away. If the other then runs at him again within the next few minutes he usually makes off without showing fight.' A study of the effects of light on mating of ebony and light strains of *Drosophila melanogaster* (Jacobs 1960) reported that male flies showed what he termed 'territorial behaviour'. Jacobs also described components of the behaviour, demonstrated that bouts between flies varied widely in duration, and showed that the behaviour itself was not seen in male flies during the first day after emerging. When marked male and female flies were placed together in a competitive situation, interactions between flies were mainly aggressive or sexual (Dow & von Schilcher 1975). The authors also described the behavioural components of wing threat, charging and boxing. In addition, great variability was seen in the numbers of times individual males were found on the food surface, attacked or were attacked, won or lost fights or copulated. These results suggested that dominant males won most of their fights and had the greatest success in mating behaviour. The most complete studies of fighting and territorial behaviour in common *Drosophila* species (*D. melanogaster*, *D. simulans*), prior to the studies from the Kravitz laboratory (Chen *et al.* 2002, Nilsen *et al.* 2004) came in 1987 (Hoffmann 1987). Following up on earlier studies (Dow & von Schilcher 1975), and using a similar experimental protocol, the components that made up fighting behaviour were defined, the proportions of time flies showed the different patterns were measured, and factors that influenced the outcome of fights were identified (Hoffmann 1987). These studies were in a complex social situation, however, in which six virgin male flies were placed in a chamber with three mated females and the ensuing social interactions were continuously videotaped for eight hours. Despite the complexity, these investigations provided a firm basis for the existence of territorial aggression in *D. melanogaster*. Even less well known was that female *D. melanogaster* also showed same-sex aggression (Ueda & Kidokoro 2002). This was confirmed when the Kravitz laboratory carried out a

quantitative analysis and a comparison of male and female aggression, highlighting the similarities and the differences in same-sex fighting behaviour in *D. melanogaster* (Nilsen *et al.* 2004).

A quantitative analysis of aggression

An examination of the genetic roots of aggression begins with an examination of the behaviour. Without understanding the 'normal' patterns of aggression in any species, including flies, it is extremely difficult to identify the consequences of any genetic perturbations that are carried out. To analyse the behaviour, a simplified arena was designed that allowed examination of agonistic encounters between pairs of animals. The arena offered resources (food, potential mates in some cases, and light to attract the flies to a central area in the arena), but also allowed room for the flies to escape from each other. Since all fly fights are different, despite the extensive inbreeding of fly lines, large sample sizes were needed to generate stable 'snapshots' of average male and female fly fights (Chen *et al.* 2002, Nilsen *et al.* 2004). For this purpose, standard methods of behavioural analyses were used, involving the generation of ethograms and the examination of how likely it was that any given behaviour changed into any other behaviour.

The results allowed a comparison of male and female patterns of aggression and showed that some behavioural patterns were shown by both males and females (approach, fencing), some were male-specific (lunge, boxing, extended wing threat), and some were female-specific (shove and head-butt). The most common patterns in the latter two categories (lunge, shove and head-butt) were subsequently used in genetic studies to characterise aggression as male-like or female-like. The flies used in the studies characterising the above behaviours were isolated in individual test tubes as pupae and therefore emerged as adults in isolation. They remained singly in tubes for 3–5 days, after which they were size-matched and paired for fights. Thus, the first time adult male or female flies encountered another fly in competition for resources was when they were paired for fights.

All of the patterns of aggression of which flies are capable are seen in these first pairings, and in all cases the behaviours and the responses of opponents are appropriate to the situation. This and other evidence not described here suggest that the establishment of the highly complex patterns of behaviour seen during aggression is largely governed by the genetic profile of the flies.

Learning and memory during fly fights

Genetics is not the whole story, however, as experience moulds the patterns of behaviour shown by winners and losers of fights during and after the time that hierarchical relationships have been established between male flies (Yurkovic *et al.* 2006). The final winner in male fights is the first fly to perform a lunge as the opponent retreats. It is as if an operant learning situation is established where one fly learns that a strategy has worked (the opponent runs away) and then uses that strategy more and more during subsequent encounters. At the end of a 30-minute fight a winner is lunging approximately 30% of the time. Losers by contrast never lunge after a decision has been made in a fight. Retreat behaviour shows a converse pattern, with losers retreating more and more as the fight progresses, while winners never retreat after a decision is reached. After a 30-minute separation period, when loser flies are paired with familiar and unfamiliar winners or with naive flies that have not fought before, the losers fight differently against familiar and non-familiar opponents. They rarely lunge against familiar opponents, but will lunge against unfamiliar opponents. Despite this difference, losers will lose all subsequent fights against all opponents except against other losers, where they can win in a small percentage of cases if they lunge against an opponent. Thus, while genes play a major role in establishing the behavioural patterns shown by flies during fights, the usage of these patterns can be modified by experience. Recent unpublished work from our laboratory suggests that the training protocol (one long fight against a single opponent versus several shorter fights against

different opponents) will influence how long flies remember that they have lost a fight. Multiple short trials are far more effective at preserving the strength of loser effects that had developed from the first fight than one long trial.

Single genes specify both how flies court and how they fight

A major reason for selecting an animal like *Drosophila* for the study of aggression, however, relates to the wealth of genetic tools that are available for use. Traditional mutants are readily available for most of the genes in the fruit fly nervous system. However, one of the most powerful tools available is the Gal4/UAS system (Brand & Perrimon 1993). This method and its variations essentially allow one to manipulate any gene desired (add foreign gene, knock out gene, change levels of gene), any place desired in the fly including within subtypes of neurons in the nervous system, and any time desired in development (up to and including inducing changes in behaving adult flies). Moreover, the genes involved in the early stages of sex determination in flies have already been identified (Billeter *et al.* 2006). These include genes that code for several splicing factors (*sex lethal* and *transformer*) and ultimately for two families of transcription factors (members of the *doublesex* and *fruitless* families) that are differentially spliced in male and female flies. The transcripts derived from the most distal promoter of the complex *fruitless* gene are spliced into sex-specific variants. In males, transcription and translation results in the formation of three or more protein forms (collectively called Fru^M), while in females the splice variants of *fruitless* are not translated into proteins. Fru^M variants are expressed in approximately 20 clusters of neurons in male fly nervous systems, which together account for approximately 2% of the total neurons in the *Drosophila* nervous system. When Fru^M is expressed in female brains, female flies are generated that court other females and that fight using male patterns of aggression (they lunge and box, but do not

show the normal female shove and head-butt patterns) – the complete description of the behavioural patterns seen in male and female fights is found in Nilsen *et al.* (2004). On the other hand, generation of the female splice variants of *fruitless* in male flies leads to males that show female patterns of aggression (Vrontou *et al.* 2006). The extended wing threat behaviour, usually a male-limited behaviour, is still only displayed by males after these manipulations. Genes involved in establishing wing threat, therefore, must be under the control of a gene (or genes) other than *fruitless*. The Gal4 system can be used to alter the sex of all or of subgroups of neurons in the nervous systems of flies (sex is cell autonomous in fruit flies) through expression of *transformer* in male flies, where it usually is not expressed, or by elimination of *transformer* expression in females (Chan & Kravitz 2007). When this is done, the same aggression phenotype is observed as when *fruitless* is altered, but, in addition, it is possible to separate clusters of Fru^M-expressing neurons into some that are essential to heterosexual courtship behaviour and some that are essential to whether flies fight like males or females. Finally, by eliminating the amine neurotransmitter (or neurohormone) octopamine (the invertebrate equivalent of norepinephrine), or by changing the sex of only the three neurons in the male-fly nervous system that normally express Fru^M and octopamine, it is possible to influence the behavioural choice between courtship and aggression (Certel *et al.* 2007).

Summary of genetic studies with *D. melanogaster*

Thus, in *D. melanogaster*, splice variants of the *fruitless* gene play essential roles in determining both how flies court and how flies fight. Therefore, in flies at least, a close relationship exists between these two usually mutually exclusive behaviours. Other genes undoubtedly will be discovered that are important to these behaviours (Dierick & Greenspan 2006, Edwards *et al.* 2006), including *doublesex*, the second transcription factor that is alternatively spliced in male and female flies. With one key gene already identified, however, a

world of new experimental approaches to the study of behaviour has been opened up through the use of this experimental model system.

7.4.2 Impulsive violence and serotonin neurochemistry in primates

Primates, including humans, are generally gregarious. Embedded in complex social hierarchies, individuals prosper with an ability to forge alliances, nurture affiliations, and enlist reliable support from fellow group members (Silverberg & Gray 1992). In many primates, high-ranking individuals are able to seize a disproportionate share of the spoils, and affirm their position with increased aggression; they initiate fights, display with attack gestures and vocalisations, and often harass subordinates. The latter tend to respond with submissive acts and calls, while they cower or flee from dominants. This is particularly true for aggressive species, such as rhesus macaques *Macaca mulatta*, where heightened impulsiveness and risk-taking may contribute to their ability to spread across inhospitable habitats and marginal conditions (Maestriperi 2007). Groups form rigid hierarchies, dominance is enforced with ferocious aggression, and opponents rarely reconcile following a fight. After the initial burst of overt aggressive activity, individuals quickly settle into their respective ranks as social structure forms and stabilises. Unambiguous hierarchies may thereby play an essential part in reducing the chronic tensions inherent to group living and, with it, a variety of stress-related pathologies (Thierry *et al.* 2004).

Most individuals of structured social groups readily cope with the need for negotiated conflict resolution (Aureli & De Waal 2000). However, a small number of juvenile males frequently attracts attention with excessive impulsive behaviour, extreme risk-taking, a distinct unwillingness to submit to stronger group members, or with displays of inappropriate aggression (Mehlman *et al.* 1994, Higley *et al.* 1996). An extensive literature across a variety of experimental scenarios supports the notion that dysfunction in serotonin neuromodulation is associated with the occurrence of abnormally high levels of overt physical aggression, suicide attempts, a lack of impulse control,

social ostracism, early migration, and a wide range of other psychiatric diagnoses and early mortality (Maes & Coccaro 1998). These behavioural pathologies of hyper-aggression strongly cluster with a range of altered measures of serotonin system function, including low titres of serotonin metabolites, reduced enzymatic activity in amine turnover, lowered serotonin receptor sensitivity, and decreased activity of serotonergic reuptake systems (see Chapter 17; Ferrari *et al.* 2005).

Despite the general association between serotonin dysfunction and inability to control violent behaviour, explanations that simply focus on absolute levels alone have failed to produce a consistent picture. Although this suggests that caution may be necessary in discussing putative links between amine neuromodulators and behaviour in general, it more likely reflects the essential constraints and properties of a dynamic modulatory system. Embedded in highly fluid networks, compensatory mechanisms constantly adjust the effectiveness of amine neuromodulators with respect to inherent set-points. Determinants of the resulting behavioural phenotype presumably reside in synaptic changes, in the magnitude, duration and temporal pattern of release, rates of inactivation, and neuromodulator ratios. The power of arousal mechanisms is thus not in determining, or producing, a behaviour. Rather, neural substrates are altered to make the emergence of a particular act more likely; neurochemical axes modulate the animal's behaviour towards adaptive responses (Libersat 2004).

Several genetic risk factors for abnormal aggression provide surprisingly strong predictability in humans and non-human primates, including a set of autosomal dominant polymorphisms in genes for the serotonin transporter and monoamine oxidase A (Retz *et al.* 2004, Wendland *et al.* 2006). As is true of behavioural and personality traits, measures of serotonin function and metabolism are strongly heritable in many primates. The serotonin transporter protein actively recycles the signalling molecule into internal sites, thereby clearing neurotransmitter from its targets. In this way it regulates synaptic serotonin concentrations and modulates the

duration of serotonergic activity (Brown & Hariri, 2006). The serotonin transporter gene in humans and rhesus macaques contains length polymorphisms in the upstream promoter region. Carriers of the short allele exhibit reduced transcriptional activity for the serotonin transporter gene, two fold lower measures of serotonin uptake, and blunted central serotonin function (Bennett *et al.* 2002). Aggression scores are also significantly higher, and an overrepresentation of the short variant is found among violent individuals (Zalsman *et al.* 2001). Hyper-aggression shows comorbidity with a range of abnormal personality traits and neurological disorders (Haberstick *et al.* 2006, Zalsman *et al.* 2006).

Consistent differences between individuals with such length polymorphisms are already observed in early infant temperament, and become more exaggerated when the individual is exposed to bad parenting and general deprivation (Newman *et al.* 2005). Illustrating the interacting influence of genotype and early rearing experiences of the developing hyper-aggressive phenotype, serotonin systems play an integral, although not yet fully understood, role.

7.4.3 Breeding lines for aggressive phenotypes

A particular trait can be transformed over time, if (1) the trait is at least partially heritable, (2) individuals exhibit variation in it, and (3) there is enhanced reproductive success associated with some variants. Charles Darwin's knowledge of the effects of selective breeding was crucial to his articulation of natural selection as a structuring process (Darwin 1859). The view that selection is as applicable to behaviour as to any morphological trait would form the basis of a bitter nature-versus-nurture argument that pitted ethologists, who endorsed the idea, against behaviourists, who denied its role (see Chapter 1; Bolhuis & Giraldeau 2004). Aside from this controversy, the presence of distinct genetic strains with enhanced levels of aggression has long been noted within a wide range of species of insects, birds, dogs, fish and mice (see Chapter 2; Sandnabba 1996). Efforts to further enhance such behaviours through selective breeding

have generally managed to produce, within a few generations, animals with levels of aggressive behaviour that greatly exceed those of controls (Nelson 2005). Our ability to create pedigrees with distinct, aggressive phenotypes represents an important tool for the analysis of genotypic variation. In addition to such selected lines, attempts to map or identify genes for aggressive behaviour have relied on outbred, inbred and recombinant inbred lines.

Arguably, no breeding programme has been maintained longer than that from which our current breeds of dogs emerged as a domesticated subspecies of the wolf *Canis lupus* (Wayne & Ostrander 2007). At least since the late Pleistocene, some 17 000 years ago, humans have continued to select dogs for qualities that make them useful as well as pleasant companions (Serpell 1995). Aimed at individuals with an overrepresentation of juvenile characteristics, such as big eyes or a playful nature, our selective control has enhanced a wide range of paedomorphic traits. Even breeds where largely adult morphologies are needed to cope with demanding work tasks, such as St Bernards or salukis, exhibit a youthful temperament that has toned down or stylised aggressive behaviour. Aggressive behaviours like barking, herding or compulsive fighting have been retained in some breeds that are commonly used for guard duties, such as rottweilers, German shepherds, German shorthair pointers and Chesapeake Bay retrievers. These are generally dominant and protective breeds, and high levels of aggression often limit their popularity within a family context. Aggressive traits are even more prominent in breeds selected for attacking prey and fighting, such as pit bull terriers (Scott 1972). The need for proper socialisation in order to prevent the emergence of problematic behaviours and human-directed aggression has contributed to the recommendation that many of these breeds should only be kept by experienced owners. In contrast, selection for demands that combine general hunting tasks with a close integration into human social companionship has given rise to breeds with calm dispositions, such as beagles, Brittany's and Labrador retrievers. In addition to such broader trends, the correlation between dog

aggression directed at other dogs and attacks on humans is relatively low, suggesting that these traits utilise, at least in part, different genetic backgrounds (Liinamo *et al.* 2007).

In mice *Mus musculus*, long-term selective breeding efforts have produced genetic lines with both altered amounts and characteristics of aggressive behaviour. A highly aggressive line of Swiss albino mice has been obtained by selecting males who scored high in an isolation-induced, inter-male aggression paradigm at 60 days of age (Turku Aggressive). Mating partners were the sisters of high-scoring males. A complementary line (Turku Non-Aggressive) has propagated only individuals with the lowest scores in the same test (Lagerspetz & Lagerspetz 1971). Although selected only for high and low aggression towards other males, behaviour varied more broadly between the lines, including measures in alternative paradigms of male aggression, territorial signalling and sexual activity, brain morphology and neurochemistry, as well as nursing competence, enhanced maze learning, and some measures of aggression in mothers.

Other breeding lines, descended from a feral population, were selected bidirectionally with attack latency as the criterion (Sluyter *et al.* 1996). Agonistic encounters between male mice occur naturally during the patrol of territorial borders, and the tests aimed to create such a context for behavioural assessment. Test males were allowed to occupy and acquire a sense of ownership of the test cage. They were then confronted with a standard, novel, male opponent who elicited offensive agonistic behaviours by his mere presence but did not initiate any attacks himself. Attack latency represents a robust behavioural measure which reliably separates individuals who attack rapidly from those who hesitate to confront the intruder. In this paradigm aggressive mice exhibit an active response towards a challenging situation, whereas non-aggressive ones cope more passively. Assigning an aggressive phenotype is to some degree contingent on the precise behavioural measure used. Even in the same paradigm, somewhat different subsets of aggressive individuals emerge if the primary measure focuses instead on the number of attacks, or on accumulated attack time. In

all of these selection efforts, significant differences between the breeding lines were obtained beginning with the second generation, and they have persisted ever since. As with other complex traits, aggression is most likely influenced by multiple genes (Plomin *et al.* 1994), although single gene effects have been noted (see below).

Increased aggression has, for instance, been linked to altered levels of expression of genes coding for amine receptors (e.g. 5-HT1B) or monoamine oxidase A (Brunner 1993). In the latter case, a rodent model demonstrates that monoamine oxidase A deficits lead to severe developmental abnormalities with an unusual aggression phenotype (Upton *et al.* 1999). In humans, possibly, one manifestation of this might be the impulsive aggression shown by males carrying a mutant form of the gene. The temptation to refer to these as mean or aggression genes should be avoided, however, because aggression is definitely not the only behavioural parameter that is altered. The ability to manipulate levels of aggression, combined with evidence from twin and adoption studies (Bartels *et al.* 2003), illustrates that links between individual differences in aggressive behaviour and genetic inheritance are contributing factors in the aetiology of aggression.

7.5 Conclusions and future directions

Attempts to define, characterise and explain aggression have generally met with considerable difficulty. This chapter has examined our current understanding of the behavioural phenomena within the context of all forms of attack, defence or threats. We have reviewed the significance of aggression in light of explanatory concepts that range from proximate to ultimate viewpoints. In summary, aggression is rarely an aberrant form of behaviour with negative consequences for all involved but, in its common expression, allows individuals to assert themselves in competition for resources. Examples of aggression span the entire animal kingdom, and its traits have been shaped by evolution like that of any other behavioural phenotype.

Aggression is clearly not a single, monolithic, behavioural category. Any attempt at explanation will critically depend on a thorough characterisation of its elemental building blocks, and it requires us to recognise the factors that control them. A better understanding of aggression will demand that we overcome the inherent difficulties in capturing the essence of an inherently multifaceted behaviour, and begin to unravel underlying elements of motivation that are not readily observed or elicited. Moreover, additional research is needed both to understand and to discover new treatments for all pathologic expressions of aggression and violence. Targeted gene deletions, RNA interference, or the generation of inducible and brain-region-specific mutants are just some of the exciting new experimental approaches for studying the role of genes, environment and their interaction in the causation of aggression. Regardless of the precise experimental protocol employed, however, success will ultimately depend on our ability to assess, precisely delineate and account for all of aggression's underlying behavioural and neural components.

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