Evolution of stress responses refine mechanisms of social rank

Wayne J. Korzan a, Cliff H. Summers b,c,d, *

a Norwegian University of Life Sciences, Oslo, Norway
b Department of Biology, University of South Dakota, Vermillion, SD 57069 USA
c Neuroscience Group, Division of Basic Biomedical Sciences, Sanford School of Medicine, University of South Dakota, Vermillion, SD 57069, USA
d Veterans Affairs Research Service, Sioux Falls VA Health Care System, Sioux Falls, SD 57105 USA

ARTICLE INFO

Keywords:
Aggression
Celerity
Decision-making
Memory
Sign stimulus
Status

ABSTRACT

Social rank functions to facilitate coping responses to socially stressful situations and conditions. The evolution of social status appears to be inseparably connected to the evolution of stress. Stress, aggression, reward, and decision-making neurocircuits overlap and interact to produce status-linked relationships, which are common among both male and female populations. Behavioral consequences stemming from social status and rank relationships are molded by aggressive interactions, which are inherently stressful. It seems likely that the balance of regulatory elements in pro- and anti-stress neurocircuits results in rapid but brief stress responses that are advantageous to social dominance. These systems further produce, in coordination with reward and aggression neurocircuits, rapid adaptive responding during opportunities that arise to acquire food, mates, perch sites, teritorial space, shelter and other resources. Rapid acquisition of resources and aggressive postures produces dominant individuals, who temporarily have distinct fitness advantages. For these reasons also, change in social status can occur rapidly. Social subordination results in slower and more chronic neural and endocrine reactions, a suite of unique defensive behaviors, and an increased propensity for anxious and depressive behavior and affect. These two behavioral phenotypes are but distinct ends of a spectrum, however, they may give us insights into the troubling mechanisms underlying the myriad of stress-related disorders to which they appear to be evolutionarily linked.

1. Function of social rank

On the high plains of Africa, where human primates are thought to have evolved (Wynn, 2004), current non-human primate residents, such as the olive baboon, live in complex and dynamic social constructs with status and stress relationships tightly interwoven (Sapolsky, 1982, 1987, 1991). Within the social hierarchy, dominant males accrue copulatory, aggressive, and food competition successes, along with unique gestural interactions. While these status parameters are highly intercorrelated, they do not correlate with aggressiveness or frequency of fighting. In fact, social dominance is also not correlated with the sex steroid testosterone (T), but is revealed by the timing and rate of change in both T and the adrenocortical stress steroid cortisol. Although plasma cortisol concentrations in dominant males are typically low, they rise rapidly and to a greater extent in response to stress, as do T levels (Sapolsky, 1982, 1983, 1988). Subordinate status results in chronically elevated plasma cortisol, with reduced testicular function and reproductive success (Sapolsky, 1985, 1988, 1989, 1990). However, during periods of social instability, adrenocortical function is modified differentially depending on the upward or downward trajectory of status (Sapolsky, 1992). Thus, social status is only temporarily stable, and its dynamic projection depends on stress-related changes in hormones and neuro-transmitters (Fig. 1) (Blanchard et al., 1995; Monder et al., 1994; Sapolsky, 1992; Summers et al., 2005a, 2005b, 2005c).

While this example from a near relative sets the stage for understanding the neurobiological mechanisms that regulate social status, the evolutionary arc for the development of the suite of adaptive behaviors that result in dominant and subordinate relationships is very wide. That is, social rank relationships are widespread among animal groups, such that hierarchies or dominant-subordinate relationships are found among invertebrates like crayfish (Huber et al., 2001) and lobster (Karavanich and Atema, 1998), and in vertebrate classes from fish to birds, rodents, elephants, and primates, including humans (Christian, 1968; DiBattista et al., 2005; Dinzbug et al., 1992; Ejike and Schreck, 1980; Greenberg et al., 1984a; Hofmann et al., 1999; Korzan and Summers, 2007; Lorenzi et al., 2009; Maruska et al., 2012, 2019; McIntyre and Chew, 1983;
Morgan et al., 2000; Nevison et al., 1996; Santamaria-Garcia et al., 2015; Semsar et al., 2001; Winberg et al., 1991, 1997; Wittemyer et al., 2008). In some species, the communal confrontations necessary to generate rank relationships produce enough emotional activation through social stress to realize cardiac health-related responses (Klemfuss et al., 1998; Sgoifo et al., 1999). Thus, the functional benefits and disadvantages of rank discrimination include such diverse aspects of fitness as daily rhythms of heart rate, body temperature, and activity, as well as reproductive success, stress responsivity, and depression (Blanchard et al., 1995; Meerlo et al., 1999; Sapolsky, 1982; Sloman et al., 2002).

Additionally, social rank relationships are not restricted by sex. Female sex rank relationships are found in numerous species, including hyenas (Lewin et al., 2014), African elephants (Freeman et al., 2010), rock hyrax (Koren et al., 2006), Bighorn Sheep (Festabianchet, 1991), reindeer (Holand et al., 2004), pigs (Hjarvard et al., 2009), rats (Militzer and Reinhard, 1983), and many types of primates (Foerster et al., 2011; Johnson et al., 2014; Kromrey et al., 2014; Lu and Borries, 2004; Renevey et al., 2013) like baboons (Mueller, 2005), chimpanzees (Riedel et al., 2020), and Rhesus macaques (Nevison et al., 1996; Zehr et al., 2005). Among mammals, some species, including elephants, hyenas, some lion prides, European bison, and bonobos have been suggested to be matriarchal, with females holding higher status and hierarchical positions. Numerous non-mammalian species also exhibit female social status hierarchies or dominant-subordinate relationships, including Jungle Fowl (Chappell et al., 1999), black-capped chickadees (Ramsay and Ratcliffe, 2003), the green anole lizard Anolis carolinensis (Andrews and Summers, 1996), and the bluehead wrasse (Price et al., 2018). In a reptilian example, females of the lizard A. carolinensis compete for access to males (Andrews and Summers, 1996). Paired females exhibit aggressive social behavior (assertion, challenge, displacement, attacks, and bites) which contributes to the development of dominant-subordinate relationships. Dominant females respond to courtship significantly more often than subordinate females, indicating receptivity. In cichlid fish, gravid females have increased sensitivity to dominant male courtship coloration (Butler et al., 2019). Dominant, typically larger, females also maintain ovarian cycling and growth (Summers et al., 1995), which is inhibited in smaller, subordinate females by the stress hormone adrenocorticotrophic hormone (ACTH) and subsequent corticosterone secretions (Summers, 1995). However, dominant status, rather than reproductive activity, appears to be regulated by heightened limbic serotonergic and dopaminergic activity in females (Summers et al., 1997) and males (Summers and Greenberg, 1995). Thus also, are stress responsiveness and resiliency, as well as reproductive success or failure, associated with social status in females and in males (Price et al., 2018; Sapolsky, 1982; Summers, 1995).

Status or rank functions as a social mechanism to coordinate behavioral output of populations when the acquisition of resources requires competition and/or evasion of predators, and is therefore stressful (Blanchard et al., 1995, 2001b; Blanchard and Blanchard, 1989b; Monder et al., 1994; Summers and Winberg, 2006; Tamashiro et al., 2005). Establishing the roles of stress neurocircuitries and molecular mechanisms associated with the establishment of social rank relationships has been facilitated by innovations in novel conceptual models, such as the Visible Burrow System, Social Defeat, Conditioned Defeat, or Stress Alternatives Model (Blanchard et al., 2015; Huhman et al., 2003; Krishnan et al., 2007; Pearson et al., 2017; Potegal et al., 1993; Robertson et al., 2015; Vaeger et al., 2020). Thus, we suggest that inter-individual rank relationships are formed and shaped by environmental and socially stressful conditions, and mediated by the neurocircuits (Fig. 1) that regulate stress and aggressive responsiveness (Summers and Winberg, 2006). For these reasons also, change in social status can occur very rapidly (Burmeister et al., 2005).

1.1. Social relationships are stressful

Although social relationships are stressful, in the classic Selye eustress/distress sense (Selye, 1984, 1985), rank relationships are stressful by the nature of status interactions (Sapolsky, 1982, 1987, 1992). It is important to begin with the idea that in populations, there are individual differences in neuroendocrine stress responsiveness (Meaney et al., 1993; Wood et al., 2010). These differences are also seen

![Fig. 1. The interactive nature of stress, aggression, reward, and decision-making neurocircuits are depicted as they exist in the mouse brain. Linear stress circuitry includes mPFC-BLA-CeA-dPAG-vIPAG, but also includes branching connections from LH/VMH-PeF, plus (not shown) to hippocampus, VTA, and nucleus accumbens (NAC). Linear aggression circuitry includes MeA & Septum-LAH/VMH/dPAG and vIPAG, but also includes AVP branches from SON, and others from mPFC and hippocampus (not shown). Ascending circuitry for decision-making includes BLA-mPFC (reciprocal neurons to stress neurons depicted), as well as branches to other cortical regions and hippocampus (not shown). Ascending Reward circuitry includes VTA-NAc (not shown) & mPFC (orange). Legend: Arginine Vasopressin (AVP) in yellow, Dopamine (DA) in orange, γ-Aminobutyric acid (GABA) in red, Glutamate (Glu) in dashed green (pro-stress) and light green (anti-stress), orexin (Orx) in purple, and serotonin (5-HT) in blue. Anatomical regions: pBLA = anterior basolateral amygdala, lCeA = lateral central amygdala, LH/DMH-PeF = orexinergic lateral hypothalamus/dorsomedial hypothalamus – perifornical Area, mCeA = medial central amygdala, mPFC = medial Prefrontal Cortex, PAG = periaqueductual gray, pBLA = posterior basolateral amygdala, SON = supraoptic nucleus, VTA = ventral tegmental area. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)](image-url)
between sexes (Bangasser and Valentino, 2012; Bangasser, 2013; Grafe et al., 2019; Valentino et al., 2012; Weintraub et al., 2010), and are influenced by individual stress histories (Vining et al., 2007). There are several additional reasons that social rank relationships may be traumatic and differentially stressful, but the primary reason is that these relationships determine the level of access to resources for each individual of a population (Blanchard et al., 1995). Those resources, such as food, water, shelter, perching/displaying/basking sites, and mates, determine not only fitness, but existence (Blanchard and Blanchard, 1989b, 1990). As such, these interactions create distress. Additionally, the social interactions that determine rank relationships are unpredictable in timing, content, and intensity (Summers et al., 2005a). While, the unpredictability of rank-determining social interactions is different for dominant as compared to more subordinate individuals, they are stressful, nonetheless, for all individuals, regardless of rank (Överli et al., 1999; Sapolsky, 1982; Summers et al., 2003). This suggests that for social species, at least, there is no aspect of life which does not involve some element of stress. Thus, the impact of stress neurocircuits on neural functions which regulate those specific aspects of life is significant. That is, social rank and the stress it generates, becomes critical elements in the life history and survival of these species, regulated by the balance of pro-stress and anti-stress components of the essential neurocircuits (Fig. 1) (Yaeger et al., 2020).

The stress neurocircuits involved in social status relationships involve three systems (Fig. 1). The first begins with reciprocal connections between basolateral amygdala (BLA) and prefrontal cortex (PFC). These areas contain both pro-stress, and anti-stress regions that can be identified by the stress-associated genetic markers Ppplr1b (DARPP32) and Rspo2 (R-Spondin 2) in BLA (Kim et al., 2016), and Drd1 (D1 receptor) in PFC (Hare et al., 2019). The BLA, which is necessary for learning related to fearful and aversive events (Orsini and Maren, 2012), is divided into anterior (aBLA expressing Rspo2) and posterior (pBLA expressing Ppplr1b) regions; with the anterior region promoting stress responses (pro-stress), and the posterior region limiting stress (anti-stress) (Kim et al., 2016). Both anterior and posterior BLA include excitatory (glutamatergic, Glu) circuits in which the BLA receives input from limbic and cortical structures, and also projects to the principal output of the amygdala, (medial portion of the Central Amygdala; mCeA), which produces learning and expression of pro-stress responses, especially to hypothalamicus and the periaqueductal gray (PAG) (Bhattacharyya et al., 2004). Inputs to the aBLA and pBLA from the PFC, come from functionally distinct sources. Pro-stress input from prelimbic PFC (PrL) projects to the pro-stress Rspo2 expressing neurons in the aBLA (Kim et al., 2016). The infralimbic (IL) portion of the mPFC projects anti-stress signaling, from dopamine receptor Drd1 expressing neurons (Hare et al., 2019), which impinge on Ppplr1b expressing neurons in the pBLA (Kim et al., 2016). This anti-stress system is promoted by second main system, dopamine (DA) activity from reward circuits that include the VTA projecting to the nucleus accumbens (NAc), but also to PFC, hippocampus, and other limbic regions (Hare et al., 2019; Lozano-Montes et al., 2019; Tovote et al., 2015). In the third system, reciprocal innervation from aBLA and pBLA designated neurons projects to specific neurons the hippocampus (Li et al., 2018; Pi et al., 2020; Yang et al., 2016), and its alternative connections to the PFC (Eichenbaum, 2017; Goldman-Rakic et al., 1984). Together, the systems reveal a pan-limbic relationship to environmental and social stress regulation (Blanchard et al., 2001a; Yang and Wang, 2017). To us it seems unlikely that any animal has a stress system that is independent of the others. Thus, social stress regulation is manifest through a balance of pro- and anti-stress systems, as well as interwoven decision-making circuitry (Fig. 1) that results in meaningful and adaptive behavioral responses (Gonzalez-Martinez et al., 2017; Smith et al., 2014; Yaeger et al., 2020; Yang et al., 2016).

The stressful effects of the establishment of social rank relationships have been demonstrated in experiments from the previously mentioned models to significantly influence, or be influenced by a large number of different, but related (through neurocircuity; Fig. 1), transmitters, neuromodulators, neurotrophins, and other factors (Table 1).

Though most of these relationships have been determined in laboratory settings, similar monoaminergic activity changes have also been demonstrated in response to social rank establishment stress in lizards in the wild (Matter et al., 1998).

1.1.1. Aggression is stressful
Of course, one of the main reasons that social interactions are stressful, is that a common element in those exchanges, especially rank-related activity, is aggression. Aggression is inherently stressful, and dangerous. Studies in all types of species demonstrate that aggressive interaction promotes stress responses from neuroendocrine systems (Blanchard et al., 1995; Lucas et al., 2004; Monder et al., 1994; Överli et al., 2004b; Smith et al., 2016; Summers, 2001, 2002; Summers et al., 2005b, 2005c; Summers and Winberg, 2006). Importantly, the activity of those neural and endocrine responses also modifies social aggression (Backström et al., 2011a; Blanchard et al., 2005; Carpenter et al., 2009; Farrokh et al., 2004; Griebel et al., 1995; Lepage et al., 2005; Överli et al., 2002a, 2002b; Schjolden et al., 2009; Wall et al., 2004a; Winberg et al., 2001). While the transmitter systems and brain regions active during social interaction/rank development stress are recapitulated in any listing related to aggression, since these two behavioral elements are typically coincidental, there are studies that examine stress responsiveness specifically during aggression. Those studies sometimes address neurotransmitter changes before the agonistic encounter (in pre-determined behavioral phenotypes), and then compare them with measurements taken during aggression (Summers et al., 2005b). There are studies that parse out temporal changes in hormone and transmitter activity, including the intervals immediately after the aggression begins (Överli et al., 1999, 2004a; Schuurman, 1986; Summers, 2001, 2002; Summers et al., 2003, 2005c). Numerous studies examine the effects of targeted drugs, and sometimes their effects in specific brain regions, to determine the neural effects on aggression itself (Backström and Winberg, 2009; Backström et al., 2011a; Blanchard et al., 1987a, 1987b; Carpenter et al., 2009; Carrillo et al., 2011; Cooper et al., 2009; de Almeida et al., 2008; de Boer and Koolhaas, 2005; Delville et al., 1996a, 1996b; Dodman et al., 1996; Ferris and Potegal, 1988; Ferris et al., 1992; Ferris, 1996; Fish et al., 2008; Grimes and Mellon, 2005; Grimes et al., 2006; Harmon et al., 2002; Harrison et al., 2000a, 2000b; Jansow et al., 2002; Larson and Summers, 2001; Lee et al., 2021; Lepage et al., 2005; Melloni and Ricci, 2010; Miczek et al., 1993, 1995, 1998; Morrison et al., 2015, 2020; Överli et al., 2002a, 2002b; Ricci et al., 2004, 2005, 2007; Schjolden et al., 2009; Schwartzter et al., 2009; Schwartzter and Melloni, 2010a, 2010b; Summers and Winberg, 2006; Veiga et al., 2007; Winberg et al., 2001). There are also a few studies in which neural and endocrine measurements are taken in the wild (Sapolsky, 1982, 1983, 1985, 1989, 1992) as well as during aggression (Matter et al., 1998). There have also been studies on aggression in captured feral rodents (Benus et al., 1991; de Boer et al., 2003; Everts et al., 1997; Sgolfo et al., 1996). The results of these studies suggest that both aggression (see section 2.3.) and stress neurocircuits (Fig. 1) are activated during aggressive bouts.

1.1.2. Definition of dominance
Social dominance is a temporary state of the highest rank, which is not genetically defined, but arises from advantages accrued through genetic and epigenetic adaptations, physiology, developmental maturation and timing, metabolic resources and reserves, temporary or long-term environmental conditions, social dynamics, and circumstance (Ricci et al., 2013). Social dominance is the key in social rank relationships, although it may be a minority position in larger social hierarchies.

1.1.3. Relationship between dominance and rank
Since rank relationships are temporary and fluid, the social
relationships and impact on stress responsiveness are somewhat dependent on the number of individuals vying for rank superiority. While most investigations into social rank in the laboratory are carried out by employing aggressive dyads, most socially competitive relationships in natural settings are more variable. What that means in terms of social stress experienced by the individuals competing is important, because, in the dyad, it is an all-or-nothing competition, and the distinctions between dominant and subordinate individuals in stress hormone and neurotransmitter concentrations are maximized, as are the patterns of their release (Summers et al., 1998, 2003, 2005b, 2005c; Summers, 2001). What is more, even among aggressive pairs, the consequences of social aggression are unpredictable and uncontrollable (Summers et al., 2005a), making this type of stressor particularly intense (Anisman and Sklar, 1981; Baratta et al., 2007; Jones and Fernyhough, 2007; Koolhaas et al., 1997a; Rozeske et al., 2011). Additional competitors and complex environmental conditions, can provide some forms of buffer for the uncontrollable and/or social stress involved (Amat et al., 2006; Christianson et al., 2009, 2011; Greenwood et al., 2005; Kiyokawa et al., 2007). For example, social play is sufficient to attenuate the effects of social stress (Burleson et al., 2016). Exercise (such as wheel running) and environmental enrichment also mitigate the effects of social defeat (Greenwood et al., 2005). One of those mitigating circumstances is the existence of territories, and the dynamics of territoriality.

### 1.1.4. The role of territoriality in social rank

There is nothing per se about social rank relationships that requires that spatial relationships for individuals or groups would also be modified, however, the price of defending resources becomes ever more costly as the range over which they must be defended grows. Thus, territoriality becomes an evolutionarily adaptive strategy, such that dominance over a territorial space reduces the cost of resource defense by decreasing interactions with conspecifics. Territorial behavior is linked to stress neurocircuitry and signaling, by which responsiveness to intrusion may be regulated (Fokidis and Deviche, 2012).

### 1.2. Stress coping strategies for social status

For all social animals, the benefits of close proximity of conspecifics is tempered by the management of agonistic socially induced stress, especially for lower status individuals. For this, species evolve stress coping strategies (Koolhaas et al., 1999, 2007, 2011; Overli et al., 2007).

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**Table 1**

| Neuroactive Element | Brain Area Influenced by Neuroactive Element to influence Social Rank | References |
|---------------------|---------------------------------------------------------------------|------------|
| AVP Amygdala (Medial) | (Albeck et al., 1997; Backstrom and Winberg, 2009; Backstrom et al., 2011b; Caldwell et al., 2017; De Goey et al., 1992; Dewan et al., 2011; Dewan and Tricas, 2011; Erhardt et al., 2009; Gesto et al., 2014; Huang et al., 2020; Larson et al., 2006; Ross et al., 2019; Shalev et al., 2011) | | |
| Hypocampus (CA2) | (Robertson et al., 2017) | |
| Hypothalamus (PVN, POA) | (Berton et al., 2006; Fanous et al., 2011; Jiang et al., 2014; Mallet et al., 2015; Moravcova et al., 2020; Naarsallah et al., 2015; Nikulina et al., 2012; Nowacka et al., 2014; Razzoli et al., 2011; Smith et al., 2014; Taylor et al., 2011) | |
| BDNF Amygdala (Basal Lateral, Central, Medial) | (Backstrom et al., 2011a; Backstrom et al., 2011b; Backstrom and Winberg, 2013; Carpenter et al., 2009; Doyon et al., 2003; Eliott et al., 2010; Fekete et al., 2009; Hostetler and Ryabinin, 2013; Kenney et al., 2004; Lukkes et al., 2005; Moltenes et al., 2016; Ruis et al., 1999; Wood et al., 2015; Wood et al., 2013) | |
| CRF Amygdala (Medial, Central) | (Backstrom et al., 2006; Korzan and Summers, 2007) | |
| Hypothalamus (VMN, POA, PVN) | (Backstrom et al., 2011a; Backstrom and Winberg, 2013) | |
| Mesolimbic DA pathway | (Korzan and Summers, 2001). What is more, even among aggressive pairs, the con | |
| (Nucleus Accumbens, VTA) | (Eagle et al., 2006; Korzan and Summers, 2007; Lucas et al., 2004; Nocjar et al., 2012; Shimamoto et al., 2011; Tidey et al., 2007; Winberg and Nilsson, 1992) | |
| Prefrontal Cortex | (Eagle et al., 2020; Mul et al., 2013) | |
| Mesolimbic DA pathway | (Berton et al., 2006; Korzan and Summers, 2007) | |
| (Nucleus Accumbens) | (Backstrom et al., 2011a; Backstrom and Winberg, 2013; Carpenter et al., 2009; Doyon et al., 2003; Eliott et al., 2010; Fekete et al., 2009; Hostetler and Ryabinin, 2013; Kenney et al., 2004; Lukkes et al., 2005; Moltenes et al., 2016; Ruis et al., 1999; Wood et al., 2015; Wood et al., 2013) | |
| Mesolimbic DA pathway | (Berton et al., 2006; Korzan and Summers, 2007; Lucas et al., 2004; Nocjar et al., 2012; Shimamoto et al., 2011; Tidey et al., 2007; Winberg and Nilsson, 1992) | |
| Nucleus Accumbens, Dorsal Striatum, VTA | (Eagle et al., 2020; Mul et al., 2013) | |
| Prefrontal Cortex (Medial) | (Eagle et al., 2006; Korzan and Summers, 2007; Lucas et al., 2004; Nocjar et al., 2012; Shimamoto et al., 2011; Tidey et al., 2007; Winberg and Nilsson, 1992) | |
| Mesolimbic DA pathway | (Berton et al., 2006; Korzan and Summers, 2007; Lucas et al., 2004; Nocjar et al., 2012; Shimamoto et al., 2011; Tidey et al., 2007; Winberg and Nilsson, 1992) | |
| Raphé (Dorsal Nucleus) | (Eagle et al., 2006; Korzan and Summers, 2007; Lucas et al., 2004; Nocjar et al., 2012; Shimamoto et al., 2011; Tidey et al., 2007; Winberg and Nilsson, 1992) | |
| Substantia Nigra | (Eagle et al., 2020; Mul et al., 2013) | |
| GABA Amygdala (Basal Lateral, Central [Medial, Lateral], Medial) | (Tsukahara et al., 2019; Xu et al., 2020; Yang et al., 2020) | |
| Hypothalamus | (Berton et al., 2006; Korzan and Summers, 2007; Lucas et al., 2004; Nocjar et al., 2012; Shimamoto et al., 2011; Tidey et al., 2007; Winberg and Nilsson, 1992) | |
| Hypothalamus | (Eagle et al., 2020; Mul et al., 2013) | |
| Mesolimbic DA pathway | (Berton et al., 2006; Korzan and Summers, 2007; Lucas et al., 2004; Nocjar et al., 2012; Shimamoto et al., 2011; Tidey et al., 2007; Winberg and Nilsson, 1992) | |
| Mesolimbic DA pathway | (Eagle et al., 2006; Korzan and Summers, 2007; Lucas et al., 2004; Nocjar et al., 2012; Shimamoto et al., 2011; Tidey et al., 2007; Winberg and Nilsson, 1992) | |
| Bed Nucleus of the Stria Terminals | (Eagle et al., 2006; Krugers et al., 1993; Park et al., 2018) | |
| Glutamate | (Kumsta et al., 2013; Smith et al., 2014; Zoicas et al., 2016) | |
| Neuropeptide S Amygdala (Basal Lateral, Central) | (Doyon et al., 2003; Panksepp et al., 2007; Sajdyk et al., 2008) | |
| Hypothalamus | (Eagle et al., 2006; Krugers et al., 1993; Park et al., 2018) | |
| Neuropeptide Y Amygdala (Basal Lateral) | (Anisman and Sklar, 1981; Bingham et al., 2011; Chajalae et al., 2013; Matter et al., 1998; Watt et al., 2004) | |
| Hypothalamus | (Anisman and Sklar, 1981; Bingham et al., 2011; Chajalae et al., 2013; Matter et al., 1998; Watt et al., 2004) | |
| Locus Ceruleus | (Eacret et al., 2019; Nocjar et al., 2012; Staton et al., 2018; Winberg and Nilsson, 1992) | |
Individual adaptive capacity and vulnerability to stress-related social conflict and disease (Koolhaas et al., 1999) has tremendous importance for understanding dominant-subordinate relationships, as both produce specific and similar behavioral phenotypes (Korzan and Summers, 2007; Øverli et al., 2007). Wild or feral populations contain individuals exhibiting proactive or reactive coping styles, playing important roles in species population ecology (Koolhaas et al., 1999), and conferring differential fitness consequences under divergent environmental conditions (Coppens et al., 2010). Divergent behavioral flexibility between phenotypes mediated by circuitry involving dopaminergic and serotonergic input to PFC (Coppens et al., 2010) is likely informed by the balance in pro- and anti-stress, motivational, and decision-making circuits (Vaeger et al., 2020). This relatively ubiquitous circuitry is capable of producing a wide variety of behavioral outcomes across a diverse array of species. One example of a common passive strategy is to change appearance, essentially allowing them to hide. For example, in the African cichlid fish Astatotilapia burtoni, non-territorial males have a specific mechanisms (Francis et al., 1993) to decrease aggressive behavior directed toward them; first by decreasing the level of body coloration exhibited and turning off the eyebar signal, thus matching female coloration these males can school with the females and hide (Korzan et al., 2009; Kittilsen et al., 2012; Lin et al., 2009; Miyai et al., 2011; Freitas et al., 2014; Høglund et al., 2000; Kittilsen et al., 2008; Parikh et al., 2006). Still other fish species, such as various salmonids, have behavioral and color changes, dictated by genetics, to cope with social stress by modifying release of stress hormones (Backström et al., 2015a; Backström et al., 2015b; Cruz and Brown, 2007; Freitas et al., 2014; Höglund et al., 2000; Höglund et al., 2002; Kittilsen et al., 2009; Kittilsen et al., 2012; Lin et al., 2009; Miyai et al., 2011; O'Connor et al., 1999; Volpato et al., 2003). Change in coloration for male A. carolinensis lizards also signals to stop aggression received (Korzan et al., 2021). Males turn from bright green to dark brown and this strategy is very powerful in stopping the aggressive behavior from the dominant animal (Greenberg et al., 1984a; Summers et al., 2005a). A more proactive behavioral coping response is escape (Arendt et al., 2012b; Dishman et al., 1997; Gallon, 1972; Horner et al., 1997; Maier, 1990; Summers et al., 2017). In the Stress Alternatives Model (SAM; see section 3.2.) (Robertson et al., 2015), designed to allow for escape during socially aggressive interactions, this behavior can be rapidly learned (Smith et al., 2014), and links this proactive behavior with reduced stress reactivity, because anxiety and stress-reducing drugs (CRF1 antagonist, ORX2 agonist) and behavior (running wheel) increase the likelihood of escape, and decrease the latency to escape (Smith et al., 2016; Staton et al., 2018). Conversely, anxiogenic stress-inducing drugs (α2 antagonist, ORX1 agonist) limit escape behavior (Pang et al., 2021; Smith et al., 2016; Vaeger et al., 2020).

1.3. Stability of social rank

One attribute of social hierarchies that is not often investigated is the stability of rank relationships among members of a group. The advantages of living in groups, such as predator avoidance, improved foraging and feeding opportunities, improved reproductive opportunities, and improved social decision-making (King and Cowlishaw, 2007; Rubenstein, 1978) provides positive pressure for the formation social hierarchies. Rank relationships must be stable enough to benefit the entire group. Stable status relationships decrease social stress, and result in more advantageous living conditions for all individuals. For the cichlid A. burtoni, stability in rank relationships is maintained through extreme levels of aggression (over 70 percent of each minute is dedicated to agonistic behavior for the first 3 h) as the sun rises, aggression is resumed by the previous day’s dominant males (Ferno, 1987; Korzan and Fernald, 2005). Other species rely, in part, on memory, such as male A. carolinensis lizards (Forster et al., 2005; Korzan and Summers, 2007; Summers et al., 2005a). Thus, stability in rank relationships can be perpetuated by multiple mechanisms, that include repeated aggression, chronobiology, and memory, and likely other mechanisms as well (such as health and fitness). As status is not permanent, despite the advantages of stability, change in rank is probably also regulated by multiple factors.

1.4. Flexibility of rank relationships

Behavioral flexibility appears to be important attribute of coping (Coppens et al., 2010) with stressful, including socially stressful conditions. Social rank produces distinctively proactive and passive phenotypes (Korzan and Summers, 2007; Øverli et al., 2007), which differ in behavioral flexibility. Proactive dominant individuals are less flexible, more rigid, behaviorally (Bolhuis et al., 2004; Coppens et al., 2010; Johansen et al., 2012; Ruiz-Gomez Mde et al., 2011), because social dominance confers advantages of course, but also because the resumption of subordinate status is more costly for former dominant individuals (Laredo et al., 2015) whose prior status marks them as a continuing threat. Despite that, rank relationships are by nature changeable, and dominant individuals are fungible. Of course, for a social system to work optimally there needs to be an appropriate amount of opportunity for individuals to increase their rank and thereby improve their overall fitness. Therefore, it is important to note that the effect of social defeat on flexibility is also determined by sex (Laredo et al., 2015). Many examples of large and long lived mammals follow an age related rank, such that social status increases with age (Pelletier and Festa-Blanchet, 2006), up to a point (Cote and Festa-Blanchet, 2001). As fitness and vigor increase, so does the possibility of elevated rank, but as health declines with age, there is an increase in rank flexibility. Simply put, the young and the old have much less opportunity to become dominant compared to animals in their prime years. Thus, health and fitness, are important factors for rank stability. In the case of A. burtoni dominant males spend a majority of their calories defending and maintaining their territory. As a result, they do not grow as fast and lose weight compared to the subordinate males. Subordinate individuals grow larger, and eventually displace dominant males (Korzan et al., 2008). Individual dominant fish will cycle through weight loss and gain, becoming dominant and subordinate many times during their lives. Dominant rainbow trout have been demonstrated to switch behavioral profiles following traumatic environmental stressors, and lose rank status (Ruiz-Gomez Mde et al., 2008). However, the offspring of the original dominant fish were also dominant, suggesting that genetic or epigenetic attributes are modifiable, at least temporarily, by environmental conditions. In male A. carolinensis lizards, individually recognized social rank carries the advantage of decreased aggression from opponents for slightly more than a week, but is lost after 10 days (Forster et al., 2005; Korzan and Summers, 2007; Summers et al., 2005a). These examples suggest that rank relationships are modifiable, by individual health, environmental, stress-related, genetic, and memory-associated mechanisms, regulated by distinctive changes in the nervous system (Burmeister et al., 2005, 2007).

1.4.1. Inflexibility associated with social dominance

Attaining dominant social rank can be energetically and/or socially expensive. In some species of lizards, where tail loss is common to avoid predators, it often comes with loss of social status, for males and females (Fox et al., 1990). Some evidence has suggested that dominant individuals are more susceptible to stress, and thus more vulnerable to depression. However, this link appears to be more closely related to loss of social rank and its resources, than to dominant status specifically (Larrieu and Sandi, 2018). For a number of species, there is no return from the loss of dominant rank status. In the insectivorous dasyurid marsupial Antechinus stuartii, dominant males exhibit intensive aggressive social interactions during territorial invasions throughout mating season. They respond with dramatic stress reactivity, and die shortly thereafter, unless they are removed from territorial interactions (Barker et al., 1978; Barnett, 1973; Bradley et al., 1980; Braithwaite, 1974). Dominant male lions have been recorded on video as suffering fatal injuries during battles to maintain status and females in the pride,
though no systematic study has determined whether this fate is common. It seems likely that in many species, loss of dominant status has dramatic consequences, which may result in mortality.

2. Social stress and aggression

2.1. Social stress is uncontrollable stress

It is important to consider that individuals involved in development of social rank relationships cannot control the amount of stress that develops from those social interactions (Summers et al., 2005a). First, the individuals involved are initially naïve to each other. Additionally, although this changes with time and experience, there is a period during which neither animal can control the reaction of their opponent. Thus, this social stress is not only uncontrollable before rank relationships are established; but is also unpredictable throughout the encounter. Even while the development of social roles during the aggressive interaction improves controllability and on average increases predictability; motivation, previous experience, and erratic foray opportunities result in unpredictable attacks from either individual.

2.1.1. The importance of unpredictable and uncontrollable stressors

Uncontrollable stressors have dramatically different effects on neuroendocrine and behavioral responsiveness from those stressors that can be controlled, resulting in potentiation of fearful responses and conditioning (Baratta et al., 2007; Der-Avakian et al., 2007; Hammack et al., 2002; Rozeske et al., 2011). The effects of uncontrollable stressors can, however, be modified behaviorally, or by the possibility of escape (Baratta et al., 2007; Greenwood et al., 2005). Despite the unpredictable and uncontrollable nature of the initial interaction, enhanced dominant or subordinate behavioral phenotypes occur as individuals of each phenotype acquire behavioral characteristics that are adaptive for continued survival. In a natural setting, subordinate animals may often control the stressor, simply by leaving. Escape is a dramatically useful behavioral option, that reduces stressful potential of interactions substantially (Carpenter et al., 2009; Smith et al., 2014; Staton et al., 2018; Summers et al., 2017). The result is that continued social interaction in captivity is an extremely stressful condition in the short term for animals that will become either dominant or subordinate, and a chronically stressful situation for subordinate individuals (Summers, 2002). Subordinate individuals denied an opportunity to evade dominant opponents may suffer from a deadly chronic stress syndrome, conditioned defeat (Huhman et al., 2003), major depression (Bjorkqvist, 2001), or its animal equivalent (Van Kampen et al., 2002). Social subordination is in some ways not unlike the uncontrollable stress paradigm that produces learned helplessness, with similar effects on stress-related systems in the brain (Fernandez Macedo et al., 2013; Greenwood et al., 2003; Greenwood and Fleschner, 2008; Hammack et al., 2002, 2012; Maier and Watkins, 2005; Petty et al., 1993, 1994a, 1994b, 1997; Vollmayr et al., 2001).

2.2. Non-aggressive behavior

Behaviors that are not explicitly aggressive play an important role in social rank attainment. There are numerous types of behavioral displays and competitive behaviors that provide evidence of aggressive intent, without being an attack, a chase, a bite, hitting, clawing, or displacement. Baring teeth and/or snarling certainly suggest aggressive motivation, but do not cause bodily injury. Psychological damage may be as potent as physical wounds for establishing dominant social rank or high hierarchical status, and emotional injury can yield long-lasting stress responsivity (Summers and Winberg, 2006). Additionally, behaviors that do not portend actual aggression, including competitive behaviors and those that signal rapid stress responsiveness, may create the needed emotional effect to produce dominant status (Andrews and Summers, 1996; Korzan et al., 2006; Summers and Greenberg, 1994; Summers et al., 1997).

Directly aggressive acts, such as biting, hitting, or clawing produces both emotional and physical wounds, but are also very costly to the individual seeking elevated social status, because they cannot be delivered without close contact (Blanchard et al., 1975, 1985; Robertson et al., 2015; Sapolsky, 1987; Smith et al., 2014; Takahashi and Blanchard, 1982). For this reason, it is evolutionarily adaptive to include displays suggesting aggressive intent in addition to actual aggression (DeCourcy and Jenssen, 1994; Greenberg, 1977; Jenssen et al., 2005). Some of these behaviors clearly signal heightened aggressive motivation, such as bearing teeth and snarling, and other aggressive displays require experience and memory to be effective, including raised hackles in feline and canine species, and extended dewlap and pushup displays in lizards. Interestingly, dewlap/pushup displays can signal both aggressive intent and mating (DeCourcy and Jenssen, 1994; Greenberg, 1977; Jenssen et al., 2005), and courtship is competitive behavior.

Competitive behavior includes any actions that focus on access to resources rather than producing physical harm. Lions protecting food resources at a kill, engage in aggressive looking behavior. Often baring teeth, roaring, and other displays are primarily associated with energy management, but also confer elevated social rank, if the displays are successful. Some behavioral displays, such as lizard dewlap extensions and pushups, are similar for aggression and reproduction. Perhaps the reason that is that both aggression and reproduction also serve to enhance social status.

Memory associated with individual recognition and identification of status is mediated by specific limbic regions of the brain, such as hippocampus and amygdala. Not surprisingly, this type of memory that is more potent with regard to social rank than other signal stimuli (Korzan et al., 2007), and is controlled by regions of the brain that are also critical for territoriality via spatial and recognition memory (Eacret et al., 2019), fear learning (Pang et al., 2021; Yaeger et al., 2020), and stress responsiveness (Smith et al., 2016).

Celerity of the stress response appears to be a critical component of elevated social rank (Korzan et al., 2006; Korzan and Summers, 2007; Sapolsky, 1982, 1983, 1988, 1989; Summers and Greenberg, 1994; Summers et al., 2005a). This relationship between rapid and brief stress neurochemical responses, but also behavioral responses, and elevated social status is evident in a wide range of vertebrates, from fish (Overli et al., 1999), to lizards (Korzan et al., 2006; Korzan and Summers, 2007; Summers, 2001; Summers et al., 2005c), and to primates (Sapolsky, 1982). For example, in the lizard A. carolinensis, rapid stress responsiveness (Summers, 2001; Summers et al., 2003) in dominant males is combined with other types of rapid behavioral responses. Feeding and courtship behaviors in dominant males follow with a much shorter latency after presentation of food or females (Korzan et al., 2006; Korzan and Summers, 2007). This relationship between increased social stress and reduced food intake is common across vertebrates, is affected by food quality and sex (Cruz and Brown, 2007; Cubitt et al., 2008; Foerster et al., 2011; Riedel et al., 2020; Ruiz-Gomez Mde et al., 2008; Ruiz–Gomez Mde et al., 2011), and is also present in salmon that emerge earlier after spawning (Vaz-Serrano et al., 2011). In this way, non-aggressive behaviors occur in a similar temporal profile in dominant individuals as aggression, and neuroendocrine stress responses (Korzan and Summers, 2007).

The behavior of individuals that eventually become subordinate can be very aggressive, at least initially (Summers, 2002; Summers et al., 2005c). However, as the establishment of social rank progresses, defensive behaviors begin to predominate (Blanchard et al., 1990a, 1990b, 1992, 1993b, 1997, 1998a, 1998b, 1998c, 2001d, 2003, 2005; Blanchard and Blanchard, 1989a; Griebel et al., 1996; Takahashi and Blanchard, 1982; Wall et al., 2004; Yang et al., 2006). These defensive behaviors signal the time when status phenotype adjustment can begin (Summers, 2002). It is important to note that chronic stress alters defensive burying behavior (Bhatnagar et al., 2003), so stress can influence behavioral phenotypes. In the SAM (see section 3.2.), there are
two distinctive behavior phenotypes in subordinate animals, Escape and Stay (remaining with the dominant opponent), suggesting that even in socially defeated animals there are pro-active and passive coping styles (Carpenter and Summers, 2009; Robertson et al., 2015; Smith et al., 2014, 2016; Staton et al., 2018; Summers et al., 2017; Yaeger et al., 2020).

### 2.3. What stimulates aggression

While aggression and behavioral displays that threaten aggression are central to the establishment of social rank relationships, the specific behavioral qualities that provoke or trigger aggression are not so well known. Aggression is displayed for a variety of reasons, and in healthy animals reserved for the last option to resolve competition for a resource (Blanchard and Blanchard, 2003). Simple presence of a competitor within territorial bounds may be sufficient unless rank-related accommodations have developed during the establishment of hierarchies. Aggressive postures provoke agonistic responses, but the definition of an aggressive posture is different for each species, and presumably for different conditions. Some signals triggering aggression are less ambiguous. In the lizard *A. carolinensis* the presence of an appropriately (green) colored moving object is not enough to stimulate aggression (Yang et al., 2001), but an active green male (without eyespots) stimulates aggressive response, whether the image is virtual (mirror or video) or real (Korzan et al., 2021). The presence of a blackened eyespot (produced by activation of β2-adrenoreceptors) (Goldman and Hadley, 1969; Goldman and Hadley, 1970; Hadley and Goldman, 1969) (in the skin behind the eye) (Summers and Greenberg, 1994) induces aggression (Korzan et al., 2000a, 2000b, 2002; Korzan and Summers, 2004), as does brown skin on the lizard, but for different reasons. Brown skin indicates submission, and rapid eyespot development indicates an opponent of dominant status. Aggression is unwarranted if the fight is already over (brown skin), or if it is one that is not likely to be winnable (faster black eyespot on opponent) (Korzan et al., 2021). Aggression begets aggression, as does previous experience (Korzan et al., 2021; Schwartz et al., 2013; Yang et al., 2001; Yang and Wilczynski, 2002). These effects produce measurable changes in the neural and hormonal systems involved in aggression and stress (Korzan et al., 2021). The neurocircuitry producing aggressive behavior (Fig. 1) will serve to suggest what triggers may be associated with aggressive attack.

The central node for inducing agonistic behavior (Fig. 1) is a region of the ventral hypothalamus extending from ventrolateral subdivisions of anterior hypothalamus (LAH) to the ventromedial hypothalamus (vVMH) (Ferris et al., 2008; Kruk et al., 1979, 1998; Lin et al., 2011; Takahashi et al., 2012). Also known as the attack area, this region receives widespread input from other elements of aggression neurocircuitry, including medial amygdala, bed nucleus of the stria terminalis, lateral septum, prefrontal cortex, and brainstem monoamine nuclei such as raphé and locus ceruleus (David et al., 2004; Delville et al., 2000; Greenberg et al., 1984b; McLott et al., 2013) that modify aggressive output (Grimes and Mellon, 2002; Haller et al., 2006; Miczek et al., 2007; Summers and Winberg, 2006; Takahashi et al., 2012). The principal aggression-related neurons of ventral hypothalamus are glutamatergic with projections to periaqueductal gray which sends efferents to motor neurons producing aggressive behavior (Fig. 1). These glutamatergic neurons are modulated directly or indirectly by vasopressinergic, dopaminergic, serotonergic, and GABAergic neurons (Ferris et al., 1997; Maxson and Canastar, 2003; Miczek et al., 2001) that produce nuanced and contextually appropriate behavior for the social and environmental conditions that exist at any given moment (Robinson et al., 2015). Aggressive behavior is stimulated by glutamatergic inputs from lateral septum and medial amygdala as well as by dopaminergic afferents and local AVP; it is inhibited by serotonergic afferents and local GABA (Ferris et al., 1997) (Fig. 1). Optogenetic stimulation of the vVMH causes male mice to attack male or female mice and even inanimate objects (Lin et al., 2011). Arginine vasopressin (AVP) in ventral hypothalamus has been associated with aggressive behavior in numerous vertebrate species including humans (Albers, 2012; Coccaro et al., 1998; Godwin and Thompson, 2012; Goodson, 2013; Heinrichs and Domes, 2008; Luppino et al., 2014). Increased expression or pharmacological activation of the V1A AVP receptor in LAH of the monogamous prairie vole facilitates aggression that is reversed by V1A and V1B antagonists (Gobrogge et al., 2009). Intranasal AVP delivery to human males increased bias toward aggressive response to ambiguous social stimuli, stimulated agonistic facial motor patterns, and increased anxiety (Thompson et al., 2006). Androgens (Yang and Wilczynski, 2002) and corticosterone (Yang and Wilczynski, 2003) have similarly been demonstrated to stimulate aggression.

Aggression stimulated in response to interaction between conspecifics occurs when an individual seeks to reinforce superior social standing, or in the case of unfamiliar conspecifics to establishing status. Critically for this kind of interaction, pyramidal neurons in the hippocampal CA2 region is the location of stored social standing memories (Leroy et al., 2018), and provides the functional link to allow aggression, since recognition actively inhibits aggression after social hierarchy is established (Korzan et al., 2007). A circuit connection between CA2 and lateral septum is selectively enhanced immediately before an attack. Vasopressinergic (AVP) enhancement of CA2 activation of lateral septum results in disinhibition of vVMH to trigger attack (Leroy et al., 2018). As the hippocampus is also a critical component of the stress neurocircuits, this direct link establishes active regulatory interaction between stress and aggression (Summers and Winberg, 2006).

### 2.4. Role of aggression in social dominance

In animal and human aggression, status and territorial control of resources provide motivations for aggressive challenge between conspecifics (Blanchard and Blanchard, 2003). More often than not, aggression is the direct precedent for social dominance, perhaps because there are long-term consequences for the outcomes of aggressive interactions (Koolhaas et al., 1997b; Meerlo et al., 1997). These types of social aggression bouts reinforce status on subordinate individuals. In addition, successful aggressive establishment of rank makes it easier for females to identify the current dominant male, who is also more successful reproductively (Sapolsky, 1982; Summers, 1995; Summers et al., 1995, 1997). This is especially true for species that use similar behaviors for aggression and attracting mates. For instance, female lizards near the aggressive arena, capable of viewing head bobs by an interacting male would recognize that individual as dominant in the area. Similarly, for other males close enough to notice the head bobs, the display also reinforces status and territorial ownership on more subordinate males.

#### 2.4.1. Winner and loser effects

A single experience of a major stressor like social defeat has long-term consequences, such that this experience acts to sensitize the defeated animal to subsequent stressors (Koolhaas et al., 1997b). Conversely, winning a competitive social interaction typically has benefits for future interactions (Dugatkin and Druen, 2004). This is most obvious when opponents are of equal size and condition. Evolutionarily, the costs are reduced when the performance of stereotypical or ritual behavioral movements become associated with aggression, and thereby limit actual aggression. Individual variation in performance may help produce contest wins, and also aid in recognition of specific individuals and their dominant status. As it is likely that these specific differences will be repeated during subsequent interactions, the behavioral effect is magnified, promoting a winner effect. In poikilotherms, like trout and lizards, the temporal aspect of these ritual behaviors seems to be a key characteristic. Individuals that initiate a variety of aggressive and non-aggressive behaviors most quickly are much more likely to win agonistic contests than individuals that are slower to react (Korzan et al., 2006; Korzan and Summers, 2007; Överli et al., 2004a, 2007; Summers, 2001; Summers et al., 2005a). Individual recognition is thought to be a
stabilizing factor for social hierarchies, such that recognition of opponents overrides winner and loser effects (Dugatkin and Earley, 2004). In the lizard A. carolinensis, memory of previous opponents, and therefore winner and loser effects have a 10 day limit (Forster et al., 2005), indicating that social recognition and memory modify aggression.

3. Social stress and decision-making

As stressful social interactions progress, opportunities to adaptively alter behavior occur repeatedly across time, and frequently allow for decision-making (Robertson et al., 2015; Smith et al., 2014). Many decision-making opportunities are associated with environmental, predatory, and social stressors, as stressful events are often the catalyst for making decisions regarding behavioral modifications necessary to temporarily adapt to novel stressful conditions. As stressful social interactions are unpredictable and uncontrollable (Summers et al., 2005a), social interactions produce numerous opportunities for this type of behavioral adaptation.

3.1. Inter-related stress and decision-making neural circuitries

Emotional and executive neurocircuitry elements, including amygdala and extended amygdala (such as bed nucleus of the stria terminalis – BNST), prefrontal cortex (PFC), cingulate cortex, nucleus accumbens, ventral tegmental area, hippocampus, paraventricular hypothalamus, are often refunctioned for numerous related purposes, such as stress, reward salience, and decision-making (Bechera et al., 2003; de Visser et al., 2010, 2011a, 2011b). These reciprocally connected regions, form circuits responsible for stress responsiveness and coping strategies, resilience or susceptibility to anxious or despair-related behavior, seeking and abusing reward (Fig. 1), producing adaptive social responses such as submissive, aggressive, or escape behaviors, and the critical decision-making that is associated with adopting these behaviors (Arendt et al., 2012a; Carpenter and Summers, 2009; Feder et al., 2009; Krishnan et al., 2007; Smith et al., 2014, 2016; Summers et al., 2017; Tanaka et al., 2012). As decision-making processes involve neurocircuitry that includes emotional and executive brain regions, they are necessarily influenced by stressors (Bechera et al., 1999; Brand et al., 2007; de Visser et al., 2010, 2011a, 2011b), and these executive functions cannot proceed exclusive of stress inputs. While the decision-making circuitry includes the amygdala, orbitofrontal cortex, anterior cingulate, dorsolateral prefrontal cortex, ventral and dorsal striatum (Bechera et al., 2003; de Visser et al., 2011a; Koot et al., 2012), these regions also regulate affect and emotional responses via specialized pro-stress and anti-stress microcircuits, which are differentiated by intracellular genetic biomarkers that are unique to the specific microcircuits (Kim et al., 2016; Yaeger et al., 2020). This suggests that stress-related circuitry that includes the amygdala (Fig. 1) is important for social decision-making (Arendt et al., 2012a; Carpenter and Summers, 2009; Smith et al., 2014; Summers et al., 2020; Yaeger et al., 2020).

3.2. Evolutionary importance of decision-making during stress

While submissive, aggressive, or avoidance responses are considered elements of anxious and depressive disorders in human populations, they are also adaptive reactions to environmental and social stressors, and thereby important factors in decisions regarding social and environmental conditions. A simple social stress decision making paradigm is the Stress Alternatives Model (SAM) which aggressively apposes two size-distinct individuals in an oval interaction arena with escape tunnels at the polar ends of the apparatus (Robertson et al., 2015; Smith et al., 2014, 2016; Staton et al., 2018). This model allows for comparison of decision-making strategies and neural function across evolutionarily disparate species, such as rainbow trout and mice (Carpenter and Summers, 2009; Robertson et al., 2015; Smith et al., 2014; Summers et al., 2017). The SAM is a Go – No Go decision paradigm in which the choice is made between 1. Egress from or 2. remaining with a significantly larger competitor during socially aggressive interactions. Interestingly, experiments using the SAM paradigm in rainbow trout and mice show identical ratios (~50/50) of Escape (egress via apical escape route) and Stay (remaining) phenotypes. Similarly, both fish and rodents require stress-reduction (via CRF1 receptor antagonist antalarmin for example) to allow stress-sensitive Stay animals to reverse behavioral phenotype and become Escape animals (Carpenter and Summers, 2009; Smith et al., 2016; Staton et al., 2018; Summers et al., 2017). Stress-promoting drugs (such as the α2 adrenoceptor antagonist yohimbine), produce behavioral reversal in animals that Escape, to become Stay phenotype individuals, or slow escape latency (Smith et al., 2016). Thus, some qualities of stress responsiveness dramatically influence decision-making, and are evolutionarily conserved.

3.3. How decision-making during stress determines social rank

The two behavioral phenotypes (Escape and Stay) expressed in SAM social interactions give evidence of multiple stress-coping strategies employed during social interaction, which result in active and passive responses (Koolhaas et al., 1999, 2007, 2011; Överli et al., 2007). Additionally, Escape animals show resilience to stress (such as in the Social Interaction/Preference test) and Stay animals exhibit vulnerability. While both groups respond to fear conditioning, the plasma corticosterone response to fear conditioning is much greater in Stay animals (Carpenter and Summers, 2009; Smith et al., 2016). Animals that demonstrate more rapid proactive responses to aggression, feeding, courtship, social displays, and stress recovery are much more likely to become dominant individuals (Fitzgerald and Kedny, 1987; Höglund et al., 2001; Höglund et al., 2005; Koolhaas et al., 1999; Korzan et al., 2006; Korzan and Summers, 2007; Korzan et al., 2021; Lailvaux et al., 2004; Överli et al., 1998; Överli et al., 2004a; Ruiz-Gomez Mde et al., 2008; Summers and Greenberg, 1994; Summers et al., 2005b; Summers et al., 2005c; Winberg et al., 1993), and social dominance has been demonstrated to be positively correlated with cognitive ability (Boogert et al., 2006). Rapid stress responsiveness of neurotransmitter (such as serotonin and dopamine activity) and stress hormone responses (corticosterone or cortisol) are key elements promoting dominant status in individuals that contend for that position (Korzan and Summers, 2007; Ling et al., 2009; Överli et al., 1999; Summers and Greenberg, 1994; Summers et al., 1998, 2003, 2005c; Summers and Winberg, 2006). The neural signaling systems that are influenced by proactive Escape phenotype include brain-derived neurotrophic factor (BDNF), cannabinoids (CB2 receptors), corticotropin releasing factor (CRF; CRF1 receptors), dopamine (DA), neuropeptide S (NPS), norepinephrine (NE, adrenergic receptors), orexin (Orx1 and Orx2 receptors), and serotonin (5-HT) (Carpenter and Summers, 2009; Robertson et al., 2015, 2017; Smith et al., 2014, 2016; Staton et al., 2018; Summers et al., 2017, 2020; Yaeger et al., 2020), suggesting that these changes may accrue to the advantage of individuals in the process of seeking dominant social status.

3.4. Established social rank modifies decision-making

For humans, primates and many other social species social rank clearly alters day to day choices of behavioral output (Abbott et al., 2003; Gong and Sanley, 2017; Sapolsky, 1991, 1992). Lizards and fish that establish social hierarchies also exhibit modified behavior based on rank relevant to a conspecific (Carpenter and Summers, 2009; Korzan and Summers, 2007; Summers et al., 2017). In male A. carolinensis with established ranks, behavioral output is changed if they are reintroduced to previous opponents (Forster et al., 2005; Korzan et al., 2007; Korzan and Summers, 2007; Summers et al., 2005a). Individuals remember each other, and they modify responses based on rank. Among territorial males of the teleost fish A. burtoni, neighbors watched and learned from
agonistic social interactions, and then modified their behavioral output based on their rank compared to animals they observed (Burmeister et al., 2005; Butler et al., 2018; Carpenter et al., 2014; Grosenick et al., 2007; Korzan et al., 2008; Maruska et al., 2013; Maruska and Fernald, 2018). Successful defeat of an opponent, promotes dominance over other males defeated by the opponent, which they attack immediately.

4. Celerity of the stress response

In the early work on social rank relationships, when stress or stress hormones were considered, the typical result reported was that subordinate individuals exhibited elevated plasma corticosterone concentrations, but dominant individuals did not. At the time, most reports suggested that the timeline of steroid secretion lasted over a period of hours or longer, and most researchers never examined the possibility that adrenal or inter-renal glucocorticoid responses could be promulgated and extinguished much faster. As circadian control of corticosterone rhythmicity began to be investigated, it was discovered that daily rhythms had a periodicity of about an hour, the frequency of which increased during stress (Lightman, 2008). Pulses were created through a transient refractory period, inhibiting HPA axis functioning following secretion, and the pulse/refractory period may be altered by changes in genetic expression, reproductive status, pain, and other life experiences (Lightman et al., 2002). This opened the door to the idea that stressor stress responses could be promoted and extinguished much faster than previously expected. Social stress stimulated by aggression between rats resulted in very rapid increases in plasma corticosterone (Schorum, 1986). Adrenal medullary responses were always known to be fast, on the order of seconds. In the lizard Anolis carolinensis, a small patch of skin just behind the eye, which densely concentrates β₂-adrenergic receptors, and responded primarily to norepinephrine (NE) (Korzan et al., 2002), responded more rapidly in male lizards that became dominant (Summers and Greenberg, 1994). Studies in trout, and in these lizards, also demonstrated that very rapid increases in plasma corticoid and brain monoaminergic activity also occurred in dominant individuals (Överli et al., 1999; Summers, 2001; Summers et al., 2003, 2005c). The data suggested that the celerity, or rapidity, of the stress response may have some functional meaning.

4.1. Functional value of rapid stress responsiveness

As experimental evidence mounted it became clear that dominant individuals had a significantly different stress response than subordinate individuals (Summers, 2002; Summers and Winberg, 2006). Under social stress conditions, which are considered to be the most intense type of stressors (Koolhaas et al., 1997a), dominant individuals have more rapid onset of behavioral (Korzan et al., 2006; Överli et al., 2004a), catecholaminergic hormonal/sympathetic (Summers and Greenberg, 1994), corticosteroid hormonal (Överli et al., 1999; Summers, 2002; Summers et al., 2003, 2005c), serotoninergic, norepinephrine and dopaminergic neurotransmitter (Ling et al., 2010; Summers et al., 1998, 2003, 2005b; Summers, 2001; Summers and Winberg, 2006; Watt et al., 2007) responses. Subordinate individuals respond more slowly for these important signaling matters, but more importantly, these systems also recover more slowly in subordinate animals as well (Överli et al., 1999; Summers, 2001; Summers et al., 2003, 2005c). The behavioral responses in individuals with more rapid onset and recovery of stress responsiveness are also more proactive, and those with slower onset and recovery exhibit behaviors that are more passive (Korzan et al., 2006; Summers et al., 2005a). Taken together, the data suggest that the rapid onset and recovery of stress responsiveness provides functional advantages that promote advancement in social rank (Korzan et al., 2006; Korzan and Summers, 2007; Överli et al., 1999, 2004a; Sapolsky, 1982; Summers and Greenberg, 1994; Summers et al., 2005b; Summers and Winberg, 2006).

4.2. Stress responsiveness modifies the plasticity of social rank

Accumulated data from the SAM paradigm demonstrates that the basic decision-making process associated with the dichotomous choice (Escape or Stay) during stressful social interactions produces relatively stable behavioral phenotypes with distinctly active (Escape) or passive (Stay) manifestations (Carpenter and Summers, 2009; Robertson et al., 2015; Smith et al., 2014, 2016; Staton et al., 2018; Yaeger et al., 2020). In other models, proactive and passive stress coping strategies are often related to dominant and subordinate rank status, respectively (Korzan and Summers, 2007; Överli et al., 2007). These phenotypes also demonstrate stress resilience for Escape animals, and stress vulnerability in Stay individuals (Staton et al., 2018; Yaeger et al., 2020). Taken together, these accumulated relationships suggest that rapid turnover of the stress response, that is, quick onset and brief duration for stress responses in dominant, active, and resilient individuals leads to the ability to more quickly return to feeding, courtship, territorial protection, and other resource acquisition behaviors after stressful encounters or conditions (Korzan et al., 2006). It is important to note that while individuals may be resilient to stress, that may not confer improved learning, especially under stressful conditions, as vulnerable Stay animals evince stronger cues and contextual fear conditioning than resilient Escape individuals (Carpenter and Summers, 2009; Smith et al., 2014; Summers et al., 2017), and other types of learning may be stronger in passive stress coping individuals or in active stress coping animals (Bolhuis et al., 2004; Coppen et al., 2010; Dalley et al., 2004). What seems evident is that critical learning events are specifically tuned to both behavioral phenotypes, and that this learning plays an important role in the phenotypic development (Pang et al., 2021), which includes social rank assessments and self-assessments. Finally, it is clear that Escape and Stay phenotypes are plastic, depending on stress-related neurotransmitter and neuropeptide actions, with more stress-sensitive individuals adopting Stay phenotypes, which are reversible by anxiolytic drugs or neuropeptides (Carpenter and Summers, 2009; Robertson et al., 2017; Smith et al., 2014, 2016; Staton et al., 2018; Summers et al., 2017, 2020; Yaeger et al., 2020). As dominant status is by definition a temporary state, we argue that stress responsiveness, as well as the learning that is associated with resilient or vulnerable phenotypes, are the primary instigators behind change in social rank.

5. Role of sign stimuli in social rank

5.1. Social signals modify behavior

Sign stimuli are typically visible behavioral releasers, under evolutionary pressure to be honest signals. Sign stimuli that relay important information about an individual’s momentary physiological state are especially powerful descriptions of condition during resource competition (Blount and McGraw, 2008; Summers, 2001; Summers et al., 2005a; Svensson and Wong, 2011). In salmonid and other fish, skin and eye color, often related to background color, have been demonstrated to influence the aggressive behavior of opponents in territorial encounters (Kelley et al., 2016; O’Connor et al., 1999; Svensson and Wong, 2011). Male A. carolinensis lizards that become dominant express eyespot signals first and maintain it longer than their opponents (Korzan et al., 2006; Korzan and Summers, 2007). This work suggests that latency to aggressive behaviors, as well as eyespot signals, are reliable predictors of future social status for individual male A. carolinensis. This is also true for the teelost species A. burtoni eyebar signal (Muske and Fernald, 1987a, 1987b). In this species the individual animal has control over the eyebar signal and expresses it while conducting aggressive behaviors,
and each fish can see when its own signal is on or off. The signal is such an honest cue that if the nerve controlling the activation of the eybar is severed on one side of the fish but not the other, the displaying dominant male will only show that side of his body while conducting aggressive behaviors (Muske and Fernald, 1987a, 1987b).

6. Memory

6.1. Social recognition, individual recognition

The critical elements in social interactions that involve territoriality or social rank include spatial memory, object recognition (Eacret et al., 2019), social recognition (Choleris et al., 2009; Ferguson et al., 2002; Kendrick, 2006; Young, 2002), and individual recognition (Couzin et al., 2002; Ferguson et al., 2002; Gheusi et al., 1994; Potts and Lewis, 2016; Tibbetts and Dale, 2007; Wiley, 2013). Recognizing spatial relationships is generally considered hippocampal function (Falkenberg et al., 1992; Morris et al., 2006; Sandli et al., 2006), in which “space cells” indicate location of the self, at least for mammals (Dubenja et al., 1999). Critically, spatial memory plays a vital role in social defeat (Eacret et al., 2019) and territorial ownership (Araya-Salas et al., 2018). However, even among invertebrate and non-mammalian vertebrates, spaces can also recognize territorial limits (Araya-Salas et al., 2018; Greenfield et al., 1989) and intrusions (Jaeger et al., 2005), social groups (De Luca et al., 2014), individuals (Gherardi et al., 2012; Karavanich and Atema, 1998), and individual rank (Aquiloni et al., 2012; Forster et al., 2005; Karavanich and Atema, 1998; Korzan et al., 2007). Importantly, this kind of individual and rank identification potently influences neuroendocrine stress responses to social challenge (Ling et al., 2010).

6.2. The primacy of memory over other determinants of social rank

For animals forming social hierarchies it is advantageous to be able to identify specific individuals with whom they have interacted (Ferguson et al., 2002). Unknown conspecífic competitors present unpredictable and uncontrollable behavioral responses (Summers et al., 2005a). For both A. carolinensis and A. burtoni, individuals immediately recognize previous combatants, their status, and adjust behavior accordingly (Fernald, 2017; Forster et al., 2005; Korzan et al., 2007; Maruska and Fernald, 2018; Summers et al., 2005a), making use of evolutionarily conserved types of behavior and neural regulatory systems (Butler et al., 2018). In A. carolinensis, eyespot celerity determines initial rank, butrematches adhere to rank memory, in spite of eyespot color (Korzan et al., 2007). For this lizard, memory is the most important component of social rank establishment for similarly sized animals, and for rank stability. In mammals, three sensory systems may be involved in determining whether a conspecific and emotional valence are remembered: auditory (of vocalizations), olfaction, and vision (Arakawa et al., 2008; Blanchard et al., 1993a; Brennan and Kendrick, 2006; Miczek et al., 1995; Parr et al., 2000). In mice and rats individual recognition (Choleris et al., 2009; Gheusi et al., 1994, 1997) of two conspecifics and their social rank results in reduced investigation (Thor et al., 1982), and no challenge (or dramatically reduced aggression), but dominant maintenance aggression occurs (Blanchard and Blanchard, 1977; Blanchard et al., 1988a, 1988b, 2001c). Thus, memory of social rank can have dramatic benefits for both dominant and subordinate individuals.

6.3. The importance of the duration of memories

If memory of a social opponent or interaction has the greatest impact on social rank, then the duration of those memories is also of prime importance for maintaining social rank. Memories, like rank, are not permanent. For example, orexin signaling during social defeat conditioning decreases subsequent social interaction and recognition performance and memory with increased anxious behavior (Eacret et al., 2019). In male green anoles (A. carolinensis) the memory of previous opponents operates to modify aggressive behavior for over a week, but then is lost after ten days of separation (Forster et al., 2005; Korzan et al., 2007; Summers et al., 2005a) and they react as if completely unaware of the opponent’s identity and status. Mammals on the other hand maintain memories of previous opponents much longer, and in the case of humans for the rest of their lives. Recently an important neural location for representation and actuation of agonistic social memories in mice has been identified (Leroy et al., 2018). Pyramidal cells in the CA2 region of the hippocampus are important for social memories; and stimulation of CA2 to lateral septum pathway, promotes social aggression. As CA2 type pyramidal cells are broadly conserved evolutionarily (Meyer et al., 2004), as is septum, it may be that this circuit is widely active in many social rank relationships.

The previous example of A. carolinensis males exhibiting approximately ten days of opponent identity and rank memory (Forster et al., 2005; Korzan et al., 2007; Summers et al., 2005a) is suggestive of the dynamism of rank relationships. Re-pairing opponents after 10 days resulted in robust agonistic encounters, with winners and losers equally successful. As winner effects are expunged, any individual has the possibility of achieving dominant status, the temporary nature of social rank is obvious for this species. In fact, memory of opponent identity and status after some period is maladaptive. We wonder if similar timelines for rank extinction exist for other lizards, birds, or mammals. If so, memories of previous opponents may be more influential for second interactions than sign stimuli or other important factors, like weight, size, or fitness, but may not be for third or fourth interactions. Therefore, the number of days after the initial interaction, may be critical information for social rank assessments.

7. Synergistic social stimuli

Cumulative effects of sensory social stimuli on interactions establishing rank relationships may be additive or synergistic (Korzan et al., 2006; Korzan and Summers, 2007; Summers et al., 2005a). Our work on the lizard A. carolinensis suggests that there are at least four stimuli that affect the rank outcomes of social interactions, including: 1. Acting Aggressively, 2. Viewing Aggressive Acts by an opponent, 3. Viewing Darkened (black) Eyespots on an opponent, and 4. Viewing Darkened (brown) Skin on an opponent (Korzan et al., 2021). Of these, the first three increase stress responsiveness, and the latter reduces it. Critically, a fifth element dramatically enhances the synergistic effect on stress responsiveness and rank outcome, and that is memory of the opponent (Korzan et al., 2007). The synergistic effect is measurable in plasma NE secretion and hippocampal serotonergic activity (5-HIAA/5-HT) and suggests a dramatic increase in emotional activation (Korzan et al., 2021). Differing degrees of emotional activation associated with different intensities of social interaction (such as dominant-subordinate interaction, dominant-dominant confrontation, or social defeat) in rats can produce relatively stronger shifts of autonomic balance toward sympathetic dominance (Gigofo et al., 1999).

7.1. Motivation to respond to stimuli

Stressful conditions drastically change outcomes of interactions with social and physical environments (Pang et al., 2021). Response to an opportunity in the physical environment, such as using an escape route to an unknown destination and resources, elevates the level of anxiety in an individual, but that apprehension becomes dramatically larger when social stress is added to the context (Carpenter and Summers, 2009; Smith et al., 2014). The Stress Alternatives model (SAM) examines this type of Go/No Go decision making in the context of aggressive social interaction (Carpenter and Summers, 2009; Robertson et al., 2015; Smith et al., 2014, 2016). Elevated social stress levels associated with a patrolling dominant individual reduces the likelihood of using an escape route to avoid that individual (Smith et al., 2016; Summers et al., 2017).
8. Predicting social rank

8.1. Anolis carolinensis Predicting social rank

The most obvious and successful way to predict the social rank of two combatants is size, larger and thus stronger individuals will win a majority of contests (Wright et al., 2019). However, regardless of size, other factors come into play; such as physical condition and species specific signals (Wright et al., 2019). In A. carolinensis a portion of skin post-orbital to each eye darkens during social interactions (Goldman and Hadley, 1969, 1976; Hadley and Goldman, 1969; Summers and Greenberg, 1994). As stated above, latency to eyespot darkening during an aggressive interaction between male A. carolinensis accurately predicts the social status of each combatant (Högblad et al., 2005; Korzan et al., 2006; Larson and Summers, 2001; Summers and Greenberg, 1994). In addition, previous experiments suggested that the first to display aggression will become dominant in dyadic interactions (Korzan and Summers, 2004; Korzan et al., 2006; Summers, 2002). However, these are characteristics of paired males while engaged in aggressive contest for social dominance. It is perhaps more remarkable that predicting social dominance is possible using behavioral motivation for experiences unrelated to social aggression. Males that become dominant court females considerably sooner, than those that become subordinate (Korzan et al., 2006). Similarly, lizards and fish that become dominant respond to food sooner (Korzan et al., 2006; Øverli et al., 2004a). These are striking relationships for seemingly unrelated events. It is advantageous to forecast social dominance, because assessing rank without aggression reduces the cost of social interaction (Summers et al., 2005b).

9. Conclusions

We suggest that the evolution of social status is inextricably linked to the evolution of stress. To understand this relationship completely, there remains a need for a greater examination of rank relationships in a diverse array of animals (Keifer and Summers, 2016). Specifically, there is a need for methods for greater examination of species-specific, stress-related, anxious and depressive behaviors, using ecologically and ethologically relevant tests that also examine motivation, decision-making, learning and memory (Carpenter and Summers, 2009; Morrison et al., 2015; Smith et al., 2014; Summers et al., 2017; Yaeger et al., 2020). As stress responsiveness is ubiquitous, the basic elements that produce social rank relationships are universally present, and widespread among both male and female animals. Social rank relationships are molded by aggressive interactions, which are inherently stressful. The neurocircuits associated with stress, aggression, reward, and decision-making interact directly and indirectly to produce these outcomes. It seems likely that the balance of regulatory elements in pro- and anti-stress neurocircuits results in rapid but brief stress responses, that are advantages to social dominance. These systems further produce, in coordination with reward and aggression circuits, rapid adaptive responding during opportunities that arise to acquire food, mates, perch sites, territorial space, shelter and other resources. This rapid acquisition of resources and aggressive postures produces dominant individuals, who temporarily have distinct fitness advantages.

Funding sources

Research reported in this publication was supported by the National Institute of Mental Health of the National Institutes of Health under Award Number R15MH104485, by a USD Center for Brain and Behavior Research (CBBRe) pilot grant, and by the Nolop Endowment via the USD Foundation to CHS. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health, the Department of Veterans Affairs or the United States Government.

CRediT authorship contribution statement

Wayne J. Korzan: Validation, Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Visualization. Cliff H. Summers: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Visualization, Supervision, Project administration, Funding acquisition.

Declaration of competing interest

The authors have no conflicts of interest to disclose.

Acknowledgements

We would like to thank Tangi R. Summers, Patrick J. Ronan, Jazmine D.W. Yaeger, Kevin T. Krupp, Jason Gale, Clarissa Staton, Russ Carpenter, Parrish Waters, Torrie L. Summers, David, Arendt, Justin Smith, James, Robertson, Menna Pratt, Tom, Andrews, Jen McKay, Aaron Emerson, Teresa Grant, Justin Achua, Jodi Lukkes, Bernard Onserio, Aaron Prestbo, Travis J. Ling, Troy Gust, Mark Gaikowski, Gary R. Ten Eyck, Oyvind Øverli, Erik Högblad, Earl T. Larson, Mick Watt, Gina Forster, John Matter, and Russell Fernald for contributing to the original work described in this manuscript. We further recognize and commend efforts in the scientific community that stand up against discrimination and social injustices. Research reported in this publication was supported by the National Institute of Mental Health of the National Institutes of Health under Award Number R15MH104485, by a USD Center for Brain and Behavior Research (CBBRe) pilot grant, and by the Nolop Endowment via the USD Foundation. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health, the Department of Veterans Affairs or the United States Government.

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