Behavioural Processes 158 (2019) 200–210

Contents lists available at ScienceDirect

Behavioural Processes

journal homepage: www.elsevier.com/locate/behavproc

Understanding zebrafish aggressive behavior

Konstantin N. Zabegalov[a], Tatiana O. Kolesnikova[a], Sergey L. Khatsko[a], Andrey D. Volgin[b,c], Oleg A. Yakovlev[b,c], Tamara G. Amstislavskaya[d,e], Ashton J. Friend[f], Wandong Bao[g], Polina A. Alekseeva[j], Anton M. Lakstygal[b], Darya A. Meshalkina[b,j], Konstantin A. Demin[b,j], Murilo S. de Abreu[h,k], Denis B. Rosemberg[i,k], Allan V. Kalueff[g,j,k,l,m,n,o,p,*]

[a] Ural Federal University, Yekaterinburg, Russia
[b] Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Russia
[c] Military Medical Academy, St. Petersburg, Russia
[d] Laboratory of Translational Biopsychiatry, Research Institute of Physiology and Basic Medicine, Novosibirsk, Russia
[e] Department of Neuroscience, Novosibirsk State University, Novosibirsk, Russia
[f] Tulane University School of Science and Engineering, New Orleans, LA, USA
[g] School of Pharmacy, Southwest University, Chongqing, China
[h] Bioscience Institute, University of Passo Fundo (UPF), Passo Fundo, RS, Brazil
[i] Graduate Program in Biological Sciences: Biochemical Toxicology, and the Department of Biochemistry and Molecular Biology, Federal University of Santa Maria (UFSM), Santa Maria, Brazil
[j] Institute of Experimental Medicine, Almazov National Medical Research Centre, Ministry of Healthcare of Russian Federation, St. Petersburg, Russia
[k] The International Zebrafish Neuroscience Research Consortium (ZNRC), Slidell, LA, USA
[l] Chemical Institute, Ural Federal University, Ekaterinburg, Russia
[m] Laboratory of Biological Psychiatry, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Russia
[n] Research Institute of Physiology and Basic Medicine, Novosibirsk, Russia
[o] Granov Russian Research Center of Radiology and Surgical Technologies, Ministry of Healthcare of Russian Federation, St. Petersburg, Russia
[p] ZENEREI Research Center, Slidell, LA, USA

ARTICLE INFO

Keywords:
Aggression
Experimental models
Zebrafish
Pharmacology of aggression
Environmental modulation

ABSTRACT

Aggression is a common agonistic behavior affecting social life and well-being of humans and animals. However, the underlying mechanisms of aggression remain poorly understood. For decades, studies of aggression have mostly focused on laboratory rodents. The growing importance of evolutionarily relevant, cross-species disease modeling necessitates novel model organisms to study aggression and its pathobiology. The zebrafish (*Danio rerio*) is rapidly becoming a new experimental model organism in neurobehavioral research. Zebrafish demonstrate high genetic and physiological homology with mammals, fully sequenced genome, ease of husbandry and testing, as well as rich, robust behavioral repertoire. As zebrafish present overt aggressive behaviors, here we focus on their behavioral models and discuss their utility in probing aggression neurobiology and its genetic, pharmacological and environmental modulation. We argue that zebrafish-based models represent an excellent translational tool to understand aggressive behaviors and related pathobiological brain mechanisms.

1. Introduction

1.1. Aggressive behaviors and related brain disorders

Aggression is a hostile agonistic behavior aiming to cause physical or psychological damage to conspecifics or other species (Brodie et al., 2016; Mazur and Booth, 1998; Nelson and Trainor 2007; Peper et al., 2015). For decades, studying aggression has mostly focused on clinical and rodent findings. However, the growing recognition of shared, evolutionarily conserved pathobiological mechanisms has fostered innovative cross-species analyses of central nervous system (CNS) traits. Therefore, studying aggression and its pathobiology may benefit markedly from utilizing a wider spectrum of model organisms. The zebrafish (*Danio rerio*) is rapidly becoming a new experimental model species in biomedicine (Lieschke and Currie, 2007) with high genetic and physiological homology with mammals, fully sequenced genome, ease of husbandry, and robust behavioral repertoire (Barbazuk et al., 2000; Howe et al., 2013, Kalueff et al., 2013). Collectively, this makes

* Corresponding author at: School of Pharmacy, Southwest University, Chongqing, China.
E-mail address: avkalueff@gmail.com (A.V. Kalueff).

https://doi.org/10.1016/j.beproc.2018.11.010
Received 2 April 2018; Received in revised form 19 November 2018; Accepted 19 November 2018
Available online 20 November 2018

Table 1
Human aggressive behavioral disorders, based on Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) (Association, 2013).

Type of disorder	Symptomology
Intermittent explosive disorder	Uncontrolled recurring outbursts of physical or verbal aggression towards objects, animals or humans
Conduct disorder	Persistent hostility toward people or animals, destruction of property, deceitfulness, propensity to thefts, and serious violation of rules
Oppositional defiant disorder	Persistent irritable or angry mood

zebrafish a useful model organism for neurobehavioral research (Kalueff et al., 2014, Egan et al., 2009). Because zebrafish also display overt aggressive behaviors (Gerlai, 2003; Ramallo et al., 2015; Oliveira et al., 2011), it is timely to consider their growing utility for probing aggression and its genetic, pharmacological and environmental modulation.

In humans, aggression has a serious deleterious impact on social life and mental health of individuals, and is often comorbid with stress, anxiety and depression (Haller and Kruk, 2006; Smith et al., 2016). In addition to human aggressive behavioral disorders (Table 1), several other psychiatric disorders with abnormal aggression include schizophrenia, psychopathy, autism spectrum disorder (ASD), alcohol-related disorder and internet gaming disorder (Association, 2013). Albeit extensively studied in clinical settings, the pathobiology of aggression remains poorly understood (Chen et al., 2012), necessitating further translational and evolutionarily relevant 'cross-species' analyses (Comai et al., 2012; Malki et al., 2016).

Human aggressive behavioral disorders are categorized as reactive or proactive, and their major symptoms include impulsivity (rapid, thoughtless acts), instability (requiring little provocation) and hyperarousal (overwhelming anxiety leading to outbursts) (Association, 2013). The reactive aggression is affective in nature, and occurs as an active hostility/rage in response to perceived provocation - unlike proactive aggression, a goal-oriented reward-motivated behavior to achieve dominance. Although these forms of aggression differ etiologically, they are highly correlated (Lobbestael et al., 2013). Both aggression subtypes are seen in various psychiatric disorders, such as schizophrenia, alcohol abuse, dementia, post-traumatic stress disorder (PTSD) and attention deficit hyperactivity disorder (ADHD) (Aman et al., 2014; Gazquez et al., 2016; Hoptman, 2015; Qouta et al., 2008; Volicer et al., 2017). While diagnosing some of them does not require aggressive phenotypes, other conditions do, as summarized in Table 1 (Rosell and Siever, 2015; Association, 2013).

1.2. Aggression pathogenesis

Mounting clinical and experimental evidence links aggression to corticolimbic-striatal circuitry (Fareri et al., 2017; Leibenluft, 2017; Repple et al., 2017), including frontal/prefrontal cortex, amygdala, hippocampus, thalamus, caudate-putamen and the nucleus accumbens (Herpertz et al., 2017; Yang et al., 2017). Amygdala-cortical and amygdala-thalamic pathways also play a role in aggression and anger (Herpertz et al., 2017). Physiological mechanisms of aggression involve aberrant monoamine neurotransmission and neuroendocrine responses (Zhang-James and Faraone, 2016; Freudenberg et al., 2016), Fig. 1. For instance, deficits in serotonin (typically caused by polymorphisms of serotonergic genes, lowered serotonin metabolism and/or tryptophan malnutrition) have long been associated with aggression in humans and animals (Umukoro et al., 2013).

Additional biomarkers of aggression include reduced dopamine signaling in the nucleus accumbens (Suzuki and Lucas, 2015) and increased adrenaline and noradrenaline in the prefrontal cortex, amygdala and hippocampus (Patki et al., 2015). Imbalance of central excitation and inhibition also triggers aggression, since higher aggressiveness correlates with reduced gamma aminobutyric acid (GABA) and higher glutamate in cortex (Ende et al., 2016), Fig. 1. Gonadal hormones are also important modulators of aggression (de Almeida et al., 2015; Gonzalez-Gomez et al., 2014), as seen in various rodent models of testosterone-driven inter-male territorial behavior (Vullioud et al., 2013). Consistent with higher melatonin in aggressive humans, its administration in animals triggers more aggression in the resident-intruder test (Liu et al., 2017). Vasopressin and oxytocin also modulate the hypothalamo-pituitary-adrenal (HPA) 'stress' hormones that trigger aggression (Fetissov et al., 2006).

Finally, genetic mechanisms play an important role in aggression, with several genes (e.g., the serotonin transporter (*SERT*), catechol-O-methyltransferase (*COMT)* and monoamine oxidase A (*MAO-A*) genes) linked to pathological aggression in both humans and rodents (Kudryavtseva et al., 2017; Lu and Menard, 2017; van Goozen et al., 2016). Other candidate 'aggression' genes include *CRHC 1* (corticotrophin releasing hormone receptor 1), *OXT/OXTR* (oxytocin/oxytocin receptor) and *AVPR 1B/1A* (arginine-vasopressin receptor) genes (Provencal et al., 2015; Waltes et al., 2016). However, the growing societal and clinical importance of aggressive behaviors (Blakely-McClure and Ostrov, 2016) faces their yet poorly understood pathobiology (Holekamp and Strauss, 2016). As animal (experimental) models are indispensable tools to study brain disorders (Cosgrove et al., 2016; Frigerio and De Strooper, 2016; Glushakov et al., 2016; McGonigle, 2014), this calls for innovative models and organisms to study aggression.

2. Behavioral models of aggression

2.1. Established models of aggression in rodents and fishes

In general, several classical aggression models in rodents include social isolation-, territorial-, maternal- and chronic stress-induced aggression (Olivier et al., 1995) (Table 2). For example, in rodent social isolation models, animals display aggressive attacks when exposed to conspecifics (Uchida et al., 2009). In the 'resident-intruder' test, aggressive interactions are provoked between a resident and an intruder animal placed into the resident's cage (Lumley et al., 2000). In the maternal aggression model, an isolated dam attacks other individuals to protect offspring from danger (Pardon et al., 2000). In the social defeat model, two animals kept in the cage (divided by a perforated screen) fight after the divider is removed, eventually producing subordinate 'losers' and aggressive 'winners' (Kudryavtseva et al., 2014). Behavioral indices of aggression in this model include the approaches to the divider (Kovalenko et al., 2014), the latency to attack, the number of attacks and total attacking time (Kudryavtseva et al., 2014).

In addition to rodents, various fish species have long been utilized in aggression research. The early studies of fish aggressiveness involved cichlids that display high sociality and territorial behavior (Barlow, 1992; Beeching, 1992). For example, the Midas cichlid (*Cichlasoma citrinellum)* commonly attack a latex dummy used as a trigger of aggression (Bond, 1992). Other fish aggression studies used coral-reef damselfish *(Pomacentrus partitus)* in a test similar to the rodent resident-intruder model (Harrington, 1995), or examined how aggression of rainbow trout *(Oncorhynchus mykiss)* correlates with dominance and elevated cortisol (Overli et al., 2004).

A popular laboratory fish species, the zebrafish is rapidly becoming an important model organism in neuroscience (Berton et al., 2012; Gerlai, 2010; McCammon and Sive, 2015) and aggression research (Gerlai, 2003; Ramallo et al., 2015; Oliveira et al., 2011), Table 3. Here,

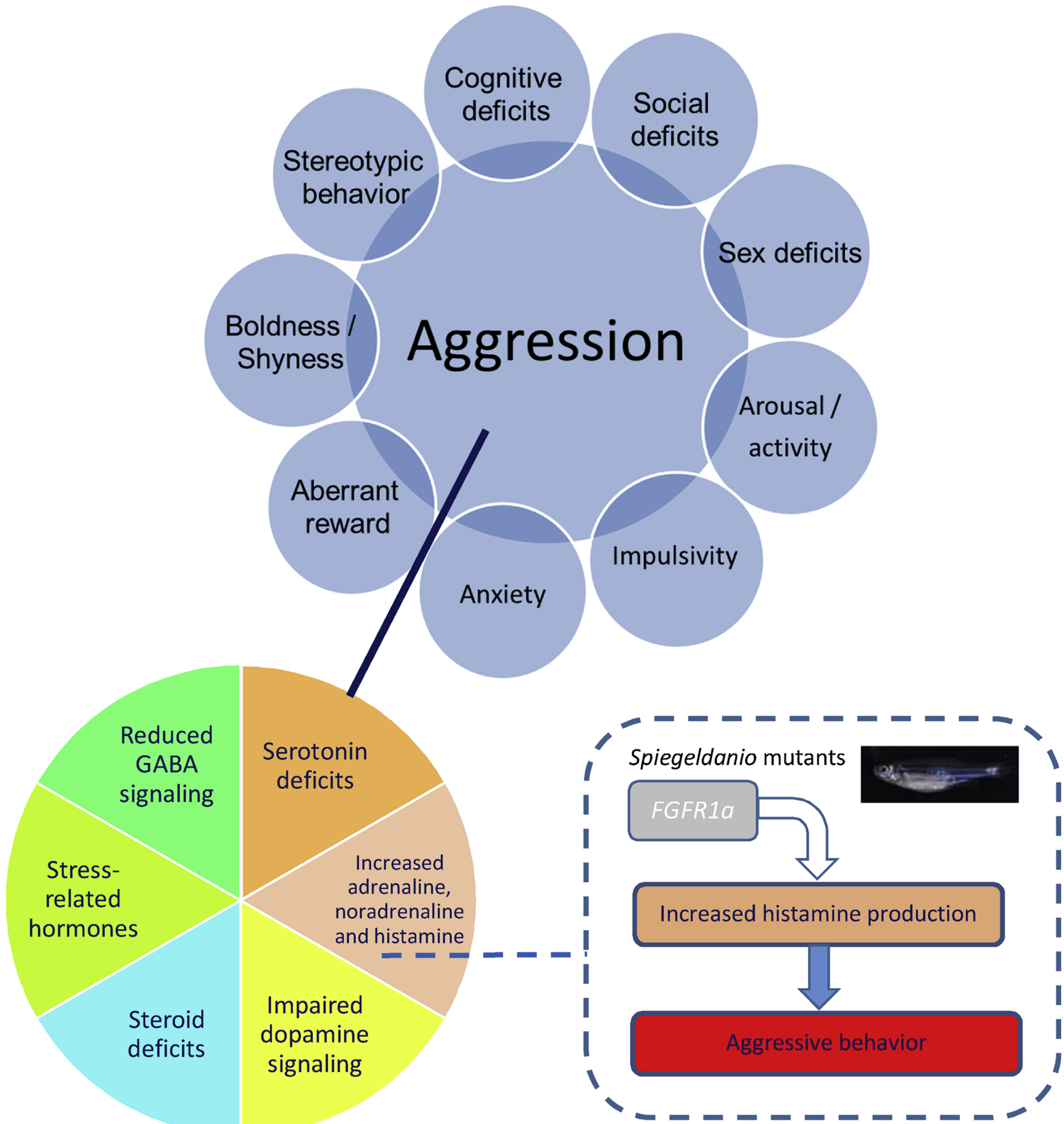

Fig. 1. Aggression as a complex phenotype with a number of underlying mechanisms (bottom) that overlaps with other major phenotypic domains as part of the putative 'Aggression + ' spectrum. Inset: Selected as an example here, zebrafish genetic model of aggression based on *Spiegeldanio* mutants. These fish under-express the fibroblast growth factor receptor 1a (FGFR-1a, that causes the inhibition of histamine synthesis), thus, showing elevated histamine and aggression (Bonan and Norton, 2015; Norton et al., 2011).

Table 2
Relevance of human aggression phenotypes (Table 1) to rodent and zebrafish models of aggression.

Human aggression	Rodent models	Zebrafish models	References
Maladaptive aggression	Cocaine-induced offensive aggression in Syrian hamsters	Real-opponent fight, mirror test (wild type AB strain)	Schwartzer et al. (2009); Teles and Oliveira (2016a, 2016b)
Chronic (persistent) physical aggression	Maternal separation, resident-intruder test, moderate prenatal alcohol exposure	Unpredictable chronic stress, mirror test (wild type)	Hamilton et al. (2014); Rambo et al. (2017); Tremblay (2008); Veenema (2009)
Occasional (intermittent) physical aggression	Operant cocaine/food self-administration, resident-intruder test (male C57BL/6 J mice)	Unpredictable chronic stress, mirror test (wild type)	Burokas et al. (2012); Rambo et al. (2017); Seguin et al. (2002)
Infancy-onset fear-induced aggression (defensive aggression)	Handling test for defensive fear-induced aggression (adult male rats)	Predator presence test (GloFish)	Ilchibaeva et al. (2017); Jha (2010); Naumenko et al. (2013)
Oppositional defiant disorder, intermittent explosive disorder	Shock-elicited fighting test (Long-Evans male rats), resident-intruder test (juvenile/adult male C57BL/6 J mice)	Social challenge, mirror test (AB strain males)	Ghiselli and Thor (1974); Leibenluft and Stoddard (2013); McLaughlin et al. (2012); Teles and Oliveira (2016a, 2016b), Wang et al. (2013)
Psychopathy (instrumental aggression)	Male-male aggressive encounters (competitive aggression; California mice)	Social challenge test, dominant-subordinate encounters (AB strain males)	Gleason et al. (2009); Louise von Borries et al. (2012); Park et al. (2018); Teles and Oliveira (2016a, 2016b)

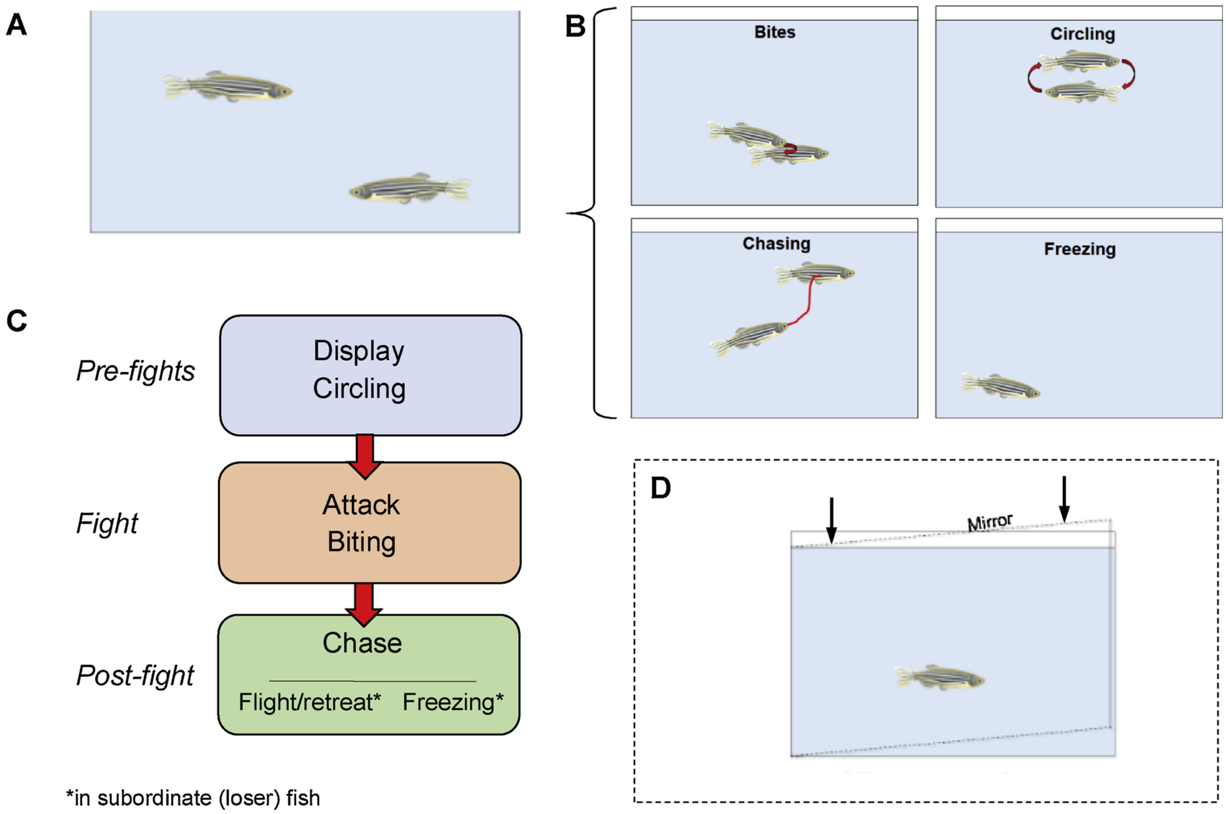

Fig. 2. Zebrafish aggression-related behaviors in the dyadic social confrontation test. Panel A shows how the fish body position within the tank in the presence of an aggressive conspecific may help interpret the outcome of an aggressive encounter, as at the end of the fight the losers usually stay near the bottom (adopting a submissive posture), or swim away (flee). Panels B and C present a typical graphical ethogram of zebrafish aggressive behavior and its behavioral organization, based on (Oliveira et al., 2011), with modifications (also see Table 4 for details). Panel D (inset) illustrates the zebrafish mirror test (see text for a detailed description; arrows denote the mirror position near the tank).

we outline the value of zebrafish for studying aggressive behaviors, focusing on *intra-species* aggression (*inter-species* aggression of zebrafish will not be discussed here).

3. Aggression in zebrafish

3.1. General mechanisms, models and tests

Aggressive behavior in zebrafish is represented by well-characterized phenotypes (Rambo et al., 2017; Oliveira et al., 2011) briefly summarized in Table 4 and Fig. 2. Such bouts typically involve hostile displays, followed by a physical attack/biting, the frequency of which increases until the losing contestant becomes submissive, and the winner dominant (Jones and Norton, 2015). Similar to vasopressin and oxytocin in rodents, their fish homologs vasotocin and isotocin are critical regulators of aggression (Terranova et al., 2017; Lindeyer et al., 2015; Tessmar-Raible et al., 2007) and social hierarchy (Larson et al., 2006; Lindeyer et al., 2015). Many other mechanisms modulate zebrafish aggression as well (Jones and Norton, 2015). For example, hypothalamus, telencephalon and some parts of metencephalon are linked to aggressive behavior and social rank in zebrafish (Filby et al., 2010). In addition, their dominance and aggression are controlled by serotonin, dopamine, histamine, somatostatin, steroids (Dahlbom et al., 2012; Filby et al., 2010, 2012) and neurotrophins (Sneddon et al., 2011).

Common signs of aggression in zebrafish include lateral displays, charges with bites and chases, eventually forcing the loser animal to retreat (Table 4, Fig. 2) (Nunes et al., 2017a; Oliveira et al., 2011). A well-established experimental test for zebrafish aggression, the mirror exposure test (Blaser and Gerlai, 2006) resembles the novel tank test (Kyzar et al., 2012), but with the inclined mirror inserted inside the apparatus (Fig. 2). Since most species fail the self-recognition test, the mirror test can be used to measure their aggression because the image reflected in the mirror is interpreted as a conspecific or rival (Gallup, 1968; Balzarini et al., 2014). Typical aggression-related endpoints in this test include time spent near mirror, the number of approaches, attempted bites and chases of mirror reflection, and the frequency of erecting the dorsal, pectoral, anal or caudal fins (Way et al., 2016). However, recent evidence supports distinct hormonal and genomic responses when fish fight real conspecific opponents vs. their own mirror images (Oliveira et al., 2016; Teles et al., 2013; Balzarini et al., 2014), thus requiring further validation of this model and its applicability to zebrafish.

Another well-established model of zebrafish aggression is the dyadic interaction test (Fig. 2), assessing fighting behavior in zebrafish dyads for a fixed period of time (e.g., in a 30-min session) (Oliveira et al., 2011). The test is usually performed in same-sex size-matched fish, assessing the frequency, the duration, the latency and the direction (who attacked whom) of all agonistic interactions from high-definition video-recordings (Oliveira et al., 2011); see Table 4 and Fig. 2 for a detailed ethogram. The test can be performed once or daily for several days, both in males and females (Dahlbom et al., 2012), typically evoking a clear dominance (Ricci et al., 2013; Oliveira et al., 2011). Aggression behaviors may become more frequent with time (Dahlbom et al., 2012) and five daily dyadic sessions may suffice to establish stable social dominant-subordinate relationships, accompanied by robust endocrine and genomic responses (Pavlidis et al., 2011). In addition, the body size may sometimes correlate with social status, as both dominant male and female zebrafish tend to be larger (Paull et al., 2010), similar to other teleost fishes (Clement et al., 2005;

Hirschenhauser and Oliveira, 2006).

Zebrafish employ social eavesdropping on aggressive interactions, and 'bystanders' can use social information to infer status of other fish in order to adjust behavior in subsequent interactions (Abril-de-Abreu et al., 2015; Cruz and Oliveira, 2015) – an interesting phenotype potentially relevant to zebrafish aggression. Furthermore, zebrafish react to environmental stimuli by changing their skin color and pigment patterns (Price et al., 2008; Nguyen et al., 2013a). As body coloration changes in zebrafish in social context and is mediated by the skin pigment cells controlled by neural and endocrine mechanisms, this phenotype is also relevant to aggression (Table 4). For example, anxious zebrafish are often pale, whereas fish following acute ethanol exposure become more aggressive and are usually darker (Gerlai et al., 2000; Fontana et al., 2016). Similarly, the size and color of zebrafish stripes and other coloration patterns (e.g., spots, color of the belly and fins) may also be affected by aggression, therefore meriting further scrutiny.

3.2. Pharmacology of zebrafish aggression

As a common animal and human behavior, aggression is highly sensitive to pharmacological treatments. For example, ethanol intake has long been associated with altered aggression in humans (Zhu et al., 2004), rodents (Quadros et al., 2014) and zebrafish, which show a dose-dependent increase in biting and chasing (Echevarria et al., 2011; Sterling et al., 2015). Furthermore, ethanol may affect aggression indirectly – e.g., by altering aggression-modulating neurotransmitters and hormones and/or upregulating their genes (Parker et al., 2014).

Relevant to the role of gonadal hormones in aggression, estrogen attenuates aggression in dominant males, turning them into 'subordinates' at high doses (Colman et al., 2009; Filby et al., 2012) (Table 3). Other compounds, such as a toxin bisphenol A (BPA), have similar effects on aggression, and are utilized in both mammalian and fish models (Kawai et al., 2003; Palanza and Parmigiani, 2017; Rosenfeld, 2015). Moreover, exposure to nickel compounds at early life stages or and sub-chronic exposure in adult zebrafish evokes anxiety, memory deficits and lower aggression (Nabinger et al., 2017). Taken together, this shows that a wide range of chemical toxins that disrupt neuroendocrine processes also affect aggressiveness and social behavior in zebrafish (Table 3). Given a well-established role of neurotransmitters in aggressive behavior (Miczek et al., 2004), there is also monoaminergic (e.g., serotonergic and dopaminergic) modulation of zebrafish aggression. For example, commonly used antidepressants, selective serotonin reuptake inhibitors (SSRIs, e.g., fluoxetine), reverse aggression in most of fish models, including zebrafish (Herculano and Maximino, 2014) (Table 3).

As already mentioned, arginine vasopressin has long been linked to aggression and dominance in mammals and humans (Albers, 2012; Fetissov et al., 2006). Therefore, a similar mechanism may mediate aggressive behavior in zebrafish (Godwin and Thompson, 2012), as dominants express vasotocin in magnocellular preoptic area, and subordinates – in parvocellular preoptic area (Larson et al., 2006). Finally, overt differences exist between dominant and subordinate fish in brain mRNA expression of genes related to stress (*crf*, *gr*, *mr*, *avt*), enzymes of aminergic pathways (tyrosine hydroxylase, DOPA decarboxylase, dopamine-hydroxylase, COMT, histidine decarboxylase) (Pavlidis et al., 2011), markers of neural activity (*bdnf, c-fos*) and serotonergic signaling (*htr2b, slc6a4b*) (Theodoridi et al., 2017).

3.3. Genetic models of zebrafish aggression

Genetic factors can determine aggressive behaviors in both humans and animals (Ferrari et al., 2005; Vassos et al., 2014). Given the ease of genetic manipulations in zebrafish (Hortopan et al., 2010; Pogoda and Hammerschmidt, 2007; Rinkwitz et al., 2011), this can be a powerful tool for studying the genetics of aggression in zebrafish. Indeed, several genetic models of zebrafish aggression have already been developed. For example, the *spiegeldanio* zebrafish mutants (Fig. 1, inset) underexpress the fibroblast growth factor (fgf) receptor 1a (fgfr1a), responsible for morphological variety in carp-like fishes (Rohner et al., 2009). However, it also controls aggressive behavior in zebrafish, as detailed genetic analyses of *fgfr1a* specific alleles and behavioral measurements (mirror test) reveal low levels of brain histamine due to reduced expression of histamine-producing enzyme gene (*hnmt*) and histamine receptors' genes (*hrh2* and *hrh3*) caused by a *fgfr1a* downregulation (Bonan and Norton, 2015; Norton et al., 2011). Thus, elevated histamine levels in the brain of aggressive zebrafish (Filby et al.,

Table 3
Pharmacology of zebrafish aggression.

Compounds	Dose, route of administration	Behavioral model, effect	References
Ethanol	10 and 20% for 10 days	Dose-dependently increased aggression in the mirror test	Sterling et al. (2015)
Ethanol	0.25% for 1 h	Increased aggression in the mirror test	Fontana et al. (2016)
Taurine	42 and 400 mg/L for 1 h	Increased aggression in the mirror test	Fontana et al. (2016)
17α-ethinylestradiol (EE_2)	50- ng/L (in ethanol) for 48 h	Reduced inter-mail aggression in two-male aggression test	Colman et al. (2009)
Bisphenol A (BPA)	10 and 500 μg/L (in ethanol) for 6 months	Reduced aggression in the mirror test	Wang et al. (2015)
Estradiol (E2)	10 and 500 μg/L (in ethanol) for 6 months	No effects	Wang et al. (2015)
Tetrabromobisphenol	5 and 50 nM* for 4 months with a 4-month detoxication	Reduced aggression in males, but not females, in the mirror test	Chen et al. (2016)
Perfluorooctane sulfonate**	2 μM at 3-120 dpf	Reduced inter-male aggression in the open field test	Jantzen et al., (2016)
Perfluorononanoic acid**	2 μM at 3-120 dpf	Increased inter-male aggression in the open field test	Jantzen et al., (2016)
Glyphosate	0.01, 0.065 and 0.5 mg/L for 96 h	Reduced aggression in the mirror test	Bridi et al. (2017)
Roundup (herbicide)	0.01, 0.065 and 0.5 mg/L for 96 h	Reduced aggression in the mirror test	Bridi et al. (2017)
Fluoxetine	50 μg/L for 15 min	Reduced aggression in unstressed, but not stressed, fish in the mirror test	Giacomini et al. (2016)
Fluoxetine	5 mg/L for 2 h	Reduced aggression in dominants and increased boldness in subordinates	Theodoridi et al. (2017)
Diazepam	16 μg/L for 15 min	No effects in the mirror test	Giacomini et al. (2016)
MK-801***	5 μM for 15 min	Decreased aggressive behavior in the mirror test	Zimmermann et al. (2016)
Ketamine	2, 20 and 40 mg/L for 20 min	Increased aggression at a low dose, decreased aggression (sedation?) at higher doses	Michelotti et al. (2018)
Oxytocin	10 ng/kg oxytocin after exposure to MK-801	Reversed effects of MK-801 on aggressive behavior in the mirror test	Zimmermann et al. (2016)
Paraquat (herbicide)	20 mg/kg i.p. 6 times over 16 days	Increased aggressive behavior in the mirror test	Nunes et al. (2017b)

* in dimethyl sulfoxide (DMSO).
** chemical waste.
*** a non-competitive antagonist of glutamate N-methyl-D-aspartate (NMDA) receptors.

Table 4
Thelist of zebrafish aggression-related behaviors (ethogram) based on the Zebrafish Neurobehavioral Catalog (ZNC) (Kalueff et al., 2013), also see Fig. 2 for illustrations.

Behavior (ZNC number)	Brief description related to the aggression context
Aggression (3)	Complex behaviors (*approach, fin raise, undulating body movement, mouth opening behavior, body color change, biting, charging, chasing* and *circling*) directed at conspecifics (or other objects) in adult zebrafish; may appear in the context of defending the territory (territorial behavior), protecting resources (e.g., females) and establishing dominance. Related to *boldness* phenotype*, can be manipulated genetically and pharmacologically
Approach (8)	Demonstration of presence and moving towards another fish (e.g., as part of *boldness* phenotype, to inspect and better size-up the opponent)
Attack (10)	Short bouts of fast swimming directed at an opponent, accompanied by *mouth opening* and *biting*; part of aggression-related behavior (differs from *strike* behavior by the presence of physical contact between fighting fish)
Biting (17)	Quick movement towards target, with mouth opening and closing, with physical contact (syn. *nipping*, 102), often occurs as fish bite each other around the gill region or fins during *fights*
Boldness (18)	Behavior characterized by bold personality trait, typically manifested in increased neophilia and risk-taking (opposite to *shyness*). Usually, bolder animals present reduced anxiety-like behavior, *body coloration* changes, more exploration and risk-taking behavior. This trait can also relate to zebrafish *aggression**
Body coloration (19)	A general change in body pigmentation resulting in a darker or lighter appearance, which can be a sign of altered aggression (e.g., during *display* or *fight*)
Charging (28)	Fast aggressive movement towards another fish with increasing acceleration, while it avoids the charger fish. This behavior helps establish social dominance and marks the resolution of a zebrafish *fight* (syn. *chase/chasing*). Charges remind *display* (see) as both involve an *approach* behavior, but occur very quickly and do not involve *fin extension* or *undulating body movements*
Chase (29)	An extended *charging*
Circling (32)	Repetitive swimming in a circular direction as part of aggressive *display*
Display (45)	Agonistic social behavior used to establish dominance/hierarchy, plays a role in *fight(ing)*. In *lateral display*, two fish line up parallel to each other head to tail, raise their dorsal fins (*fin extension*), extend caudal fins, darken in color (*body coloration*) and swim in circles (circling). During *frontal display*, two fish approach each other from the front with the attempt *charging* and/or *biting.*
Fight (58)	Agonistic confrontation between two individuals often used to establish social dominance; comprises two distinct phases: the fish first assess each other by exhibiting *display, mouth opening* and *biting*, which continues until the first chase/flee occurs. Next, the 'winner' (chaser) initiates other agonistic behaviors, while the 'loser' displays *submission behavior* or *freezing*
Fin extension, erection (60)	Raising the dorsal fin and/or extending the caudal fins; common in zebrafish during aggression
Fleeing (61)	Accelerating movement away from an aggressive fish during *fight, display* or *chase* (syn. *flight*, 63), also see *retreating*
Flick (62)	An agonistic behavior observed when two zebrafish swim towards each other, briefly touch mouths, and then simultaneously 'flick away' in opposite directions; can be repeatedly displayed during *fight*
Freezing (68)	Remaining immobile during/after social interactions, often with retracted fins, representing a typical *submissive behavior* of subordinate fish (e.g., after *fight*)
Mirror stimulation response (98)	Complex behaviors evoked in fish by mirror exposure, linked to *aggression* and typically includes *approach*, headbutting, *biting* (the mirror) or *chasing* own reflection (*reflection chasing)*
Mouth opening (100)	Frequent mouth opening (different from chewing or *biting*) as part of aggressive *display* or *attack,* likely serving to intimidate the opponent
Reflection chasing (126)	Chasing own reflection in the mirror test as part of the *mirror stimulation response*
Retreating (129)	An agonistic *fleeing* behavior when a submissive fish swims rapidly away from the opponent (dominant fish) in response to an *attack* (e.g., after a *striking, biting* or *chasing*)
Shyness (142)	A personality trait with lower exploratory and motor activity, neophobia, reduced risk-taking behavior (opposite to *boldness*), can be associated with reduced *aggression**
Striking (160)	An aggression-related behavior, observed in zebrafish when the fish swims rapidly toward the opponent, but without physical contacts between them. Differs from approach by a generally much higher velocity and its aggressive (rather than investigatory) nature (also see *attack*, which occurs with physical contact)
Submissive behavior (162)	A common social behavior following aggressive confrontations: submissive zebrafish stays immobile (with fins retracted), typically near the bottom of the tank, often with the caudal part of the body oriented downward (tail dip)
Territorial behavior (172)	Monopolization and aggressive defense of a defined area of habitat (e.g., trespassers into the territory may be chased or bitten by the dominant aggressive fish, but can *fight* to challenge its dominance)
Undulation (182)	A wave-like or snake-like undulating body motion as part of aggression-related behaviors, which occurs mainly at the beginning of *fight* before *charging*, especially between two opponents equal in size. This behavior is likely related to the use of lateral line to size-up the opponent by the waves it generated, but may also represent a *display*, in order to intimidate the opponent

* See interesting discussion on aggression-boldness correlation in (Martins and Bhat, 2014).

2010) may be due to *fgfr1a* under-expression, because *fgfr1a* lowers histamine synthesis (Bonan and Norton, 2015).

Likewise, endocannabinoids also modulate animal and human aggressive behavior (Mechoulam, 2002). For example, fatty acid amide hydrolases (FAAH1, FAAH2) and monoacylglycerol induce aggressive behavior in male mice acting via endocannabinoid CB1 receptors (Aliczki et al., 2015). Similar to mammals, zebrafish express the *faah* and *faah2* genes (McPartland et al., 2007) and while their knockout evokes anxiety-like behavior (Krug et al., 2018), assessing aggression in these mutants may further probe the role of central endocannabinoids in zebrafish aggression.

Some signal molecules, such as nitric oxide (NO), also affect animal behavior (Mutlu et al., 2009; Umathe et al., 2009) by modulating monoaminergic neurotransmission (Kiss, 2000; Lopez et al., 2005). Zebrafish NO synthase mutants (*nos1*$^{-/-}$) are less aggressive and more anxious, whereas treating them with the serotonin 1 A receptor agonist 8 – OH-DPAT reverses these phenotypes (Carreno Gutierrez et al., 2017).

3.4. Environmental modulation of zebrafish aggression

Environmental enrichment has long been used to reduce aggression in laboratory animals (Friske and Gammie, 2005; Marquez-Arias et al., 2010; Sherwin et al., 1999; Van Loo et al., 2003), and is now applied to zebrafish models as well. For example, exposing two 'wild-derived' (U and PN) and one laboratory-bred (SH) zebrafish populations to various environments shows that vegetation enrichment increases aggression in population-dependent manner (Bhat et al., 2015). Supporting the role of social enrichment in zebrafish aggression, both male and female zebrafish (kept in pairs with same-sex peers) quickly develop dominant-subordinate relationships in all pairs (Paull et al., 2010), but show fewer aggressive interactions after a 1-week enrichment (Wilkes et al., 2012). Moreover, monoaminergic modulation of aggression depends on social enrichment context (Dahlbom et al., 2012). For example, male dyadic interactions, but not the mirror test procedure, rise telencephalic serotonin and dopamine activity in dominant fish, and optic tectum serotonin activity in subordinates (Teles et al., 2013).

Table 5
Selected outstanding questions in zebrafish aggression research.

Questions
Do aggressive behaviors differ in laboratory strains vs. wild-derived vs. wild-caught zebrafish?
Do aggressive behaviors differ between laboratory-tested wild zebrafish vs. fish in their natural habitat?
How does domestication influence zebrafish aggression across various zebrafish strains?
Do different populations of zebrafish in the wild express overt stable baseline differences in aggressive behaviors?
Does zebrafish intra-species aggression correlate with their aggression towards similar (e.g., *Danioid*) fishes?
How to characterize the aggressive behavior in different fish 'personalities'?
How can zebrafish social hierarchy modulate their aggressiveness?
What are 'early' behavioral and physiological predictors or risk factors of subsequent aggression as adults?
How to best characterize zebrafish social environment to predict the individual phenotype of aggressiveness?
At what level can the breeding mode trigger reactivity to aggressive behavior?
Can zebrafish housing/husbandry conditions trigger or minimize aggression?
What neural mechanisms and circuits are involved in aggressive-related phenotypes in zebrafish?
Can distinct genes differentially modulate aggressive behavior in different behavioral tasks?
Are there robust and stable individual differences in baseline aggression of zebrafish?
Do aggressive behaviors consistently differ among zebrafish strains?
How do zebrafish express their inter-strain aggression?
Do locomotor activity levels and impulsivity traits correlate with aggression in zebrafish?
Which behavioral endpoints are shared (or correlated) in distinct tasks assessing fish aggression?
Do zebrafish habituate to their virtual opponent image in the mirror test?
Is zebrafish a useful organism for modeling fear-induced aggression?
Can zebrafish mimic aggression in neurodegenerative disorders, such as Alzheimer's and Parkinson's diseases?
Is the mirror task a suitable protocol to predict aggressive behavior after pharmacological manipulations?*
How can anxiolytic and anxiogenic treatments influence aggressive-related phenotypes in zebrafish strains?
What are potential epigenetic mechanisms of aggression modulation in zebrafish models?
Are there new 'candidate' aggression genes in zebrafish models?
What genes and other experimental factors are associated with pathologically high (e.g., killer-type) aggression in zebrafish?
Can zebrafish help develop experimental models of sociopathic personality, pathological violence and 'serial killer' behavior?
What specific behavioral or physiological factors can trigger male aggression towards female zebrafish (and vise versa)?
What genes and other experimental factors are associated with pathologically low aggression in zebrafish?
What zebrafish behaviors can trigger intra-species aggression in same-sex pairs and in the opposite sex?
Are there behavioral or biological differences between intermale vs. interfemale aggression in zebrafish?
How relevant are existing models of zebrafish aggression to human mental disorders with aberrant aggression?
How can we objectively compare zebrafish aggressive behavior with the human aggression-related behaviors?
Does sexual experience potentiate zebrafish aggression (e.g., similar to how it does in rodents)?
How does aging affect aggression in zebrafish?
Do underlying biological mechanisms differ if aggression is directed against juvenile (vs. adult) fish?
Are there specific behavioral and physiological markers of adult aggression directed at juvenile zebrafish?
Are there specific behavioral and physiological biomarkers of parental aggression in zebrafish?
As clear dominance is established in most, but not all groups, what factors may contribute to this phenomenon?
Are there fish-specific (vs. shared) circuitry controlling zebrafish aggression that do not have close analogs in humans and mammals?

* Note a complex nature of the mirror test behavior, showing species-specific correlation with aggression (e.g., see (Balzarini et al., 2014) for discussion).

4. Some existing challenges

Clearly, zebrafish models of aggression are far from being well-established, and many open questions remain (Table 5). For example, although zebrafish are social animals that form shoals, they show higher aggression and dominance when in pairs (Teles and Oliveira, 2016a, 2016b). Thus, further studies are needed to explore which zebrafish behavioral endpoints reflect aggression *per se* vs. other related behavioral domains, such as activity, sociality or impulsivity (Table 5). Similarly, the shy-boldness continuum in zebrafish (Table 4) can be relevant to aggression (Way et al., 2015; Martins and Bhat, 2014) and be critical for animal survival (Ariyomo et al., 2013). Unlike shy individuals, bold zebrafish typically display high novelty exploration, risk-taking behavior and low anxiety (Kalueff et al., 2013; Wright et al., 2003). While some studies fail to link zebrafish boldness to aggression (Way et al., 2015), markedly more evidence supports such link in laboratory-raised (Rey et al., 2015; Dahlbom et al., 2011), wild-caught (Martins and Bhat, 2014) and genetically modified zebrafish (Norton et al., 2011). Furthermore, fish boldness can predict dominance in subsequent dyadic confrontations (Dahlbom et al., 2011), and so it can be used as an additional 'proxy' endophenotype associated with zebrafish aggression. This may allow widening the focus of zebrafish aggression research to include both direct measures of aggression and associated traits (e.g., activity, dominance and boldness) as part of a broader 'Aggression + ' behavioral syndrome (Fig. 1).

Recent advances in computer-based neurophenomics include analyses of social behaviors in multi-fish groups (Green et al., 2012), automatic testing of aggression in multiple animals per trial (Carreno Gutierrez et al., 2017) and high-throughput neurophenotyping of multiple behavioral traits (e.g., exploration, boldness, aggression and sociability) (Fangmeier et al., 2018). Clearly, these and future sophisticated computer-based tools will continue to foster zebrafish aggression research, consistent with recent 'integrative', cross-domain animal models (Stewart and Kalueff, 2015; LaPorte et al., 2010) that simultaneously target several overlapping neurobehavioral domains (Kalueff et al., 2015, 2008). This strategy will also better reflect the clinical picture of human aggressive behavioral disorders (Table 1) that often share other phenotypes (beyond aggression) with a wide spectrum of brain illnesses, such as psychoses, attention deficit hyperactivity disorder and pathological impulsivity (Jones and Norton, 2015). Likewise, zebrafish can recognize the previously exposed conspecifics, demonstrating a long-term social memory (Madeira and Oliveira, 2017). Thus, putting fish social memory in the context of aggressive behavior may help understand whether zebrafish equally well remember a winner vs. loser, or show differential social memories for positive and negative social experiences. Further research may clarify the duration of their social memory retention, as well as examine in detail any individual, age-, sex- or strain- differences in these cognitive processes related to aggression.

Another related question here is, to what extent such individual social experiences can shape subsequently developing zebrafish aggression phenotypes? Current evidence suggests that such relationships between social status and aggression in zebrafish may be nonlinear, and depend on individual coping strategies. For example, following dyadic social confrontations, winners may increase the probability of winning subsequent fights without changing their fighting behavior, whereas losers may lower this probability by decreasing the motivation to escalate fights (Oliveira et al., 2011). Likewise, recent studies show that male Siamese fighting fish (*Betta splendens*) monitor aggressive interactions between neighboring conspecifics and use this information to estimate fighting ability in their own subsequent aggressive interactions with the observed individuals (Oliveira et al., 1998). Such 'social eavesdropping' ability exists in zebrafish as they pay more attention to fighting vs. non-fighting conspecifics (Lopes et al., 2015; Abril-de-Abreu et al., 2015). Thus, social and cognitive factors, such as memories of prior individual experiences, become important for studying aggressive behaviors in zebrafish. Translationally relevant, such integrative models in zebrafish fit with a recent US NIH cross-disorder Research Domain Criteria (RDoCs) initiative to reconceptualize psychiatric disorders into transdiagnostic functional dimensional constructs based on neurobiological measures, biomarkers and observable behaviors (Kelly et al., 2018; Veroude et al., 2016). As RDoCs have already been successfully applied to studying human aggression (Verona and Bresin, 2015; Sukhodolsky et al., 2016; Fonagy and Luyten, 2017), the possibility of developing similar cross-domain 'integrative' models of aggression in zebrafish becomes important.

Furthermore, while animal models of CNS mechanisms traditionally focus on neurobehavioral phenotypes, there is a growing recognition of pathophysiological overlap between metabolic and mental disorders in various model organisms, including zebrafish (Nguyen et al., 2013b). As zebrafish continue to demonstrate a strong potential for modeling human brain and metabolic disorders, as well as their comorbidity (Nguyen et al., 2013b), monitoring fish metabolic profiles in addition to their aggression and stress coping can be interesting. Indeed, compared to stress-prone 'reactive' individuals, the stress-resistant 'proactive' zebrafish are more aggressive, have higher metabolic rates and show lower anxiety (Yuan et al., 2018). Thus, a broad spectrum of zebrafish aggression-related phenotypes may eventually be expanded even further, to include non-brain physiological responses, such as metabolic profiles.

As already mentioned, genetic factors play an important role in human and zebrafish aggression (Jones and Norton, 2015; Ariyomo et al., 2013), accompanied by altered gene expression patterns in clinical and animal models (Malki et al., 2016). For example, of 70 genes differentially expressed in fight-exposed vs. isolated zebrafish, 7 genes are homologous to those differentially expressed in aggressive vs. non-aggressive mice. Mainly centering around the *c-fos* molecular hub and MAPK signaling pathway, these genes reveal conserved cellular networks implicated in aggressive behaviors (Malki et al., 2016); also see similar brain transcriptomic findings in zebrafish observing fighting vs. non-fighting zebrafish pairs (Lopes et al., 2015). Collectively, this calls for further genomic studies of zebrafish aggression.

Additionally, epigenetic regulation of aggression has already been reported in humans (Waltes et al., 2016) and fish, implicating several genes, such as *fgfr1a* (Norton et al., 2011) and histone deacetylase 4 (*hdac4*) (Malki et al., 2016), in zebrafish aggression. Since human *HDAC4* is associated with aggressive behavioral disorders, linking its homolog to zebrafish aggression supports the evolutionarily conserved epigenetic mechanisms of aggression. Finally, questions related to sex differences in zebrafish in aggression still remain open (Table 5), as both male and female zebrafish establish dominant-subordinate relationships (Reolon et al., 2018), but seem to differ in their aggressive behaviors (Ariyomo and Watt, 2013).

5. Concluding remarks

In summary, zebrafish have demonstrated their growing utility in biological psychiatry (Kalueff et al., 2014), and are now emerging as a promising tool to study aggression (Oliveira et al., 2011; Teles and Oliveira, 2016a, 2016b). Zebrafish can also help analyze aggression in models that cannot be fully established in other species (Table 2). For example, the mirror test is highly suitable to evaluate zebrafish aggressive behavior, as it does not cause physical harm in experimental subjects (Norton and Bally-Cuif, 2010) and accurately records a simple set of easy-to-interpret behavioral traits (Jones and Norton, 2015). Given their extensive behavioral repertoire (Kalueff et al., 2013), studying multiple zebrafish agonistic behaviors (Table 4) can reveal novel neural mechanisms underlying aggression and social hierarchies in this species (Oliveira et al., 2011; Teles and Oliveira, 2016a, 2016b).

Finally, considering the 3R principles of humane bio-experimentation, fish as simpler organisms may be more suitable ethically for testing 'stressful' aggressive behaviors than mammals (Fontana et al., 2018), especially as fish also tend to cause a lesser harm to conspecifics during fights, since their bites induce less tissue damage than biting wounds in rodents. Collectively, this supports a wider application of zebrafish models to probe aggression biology and pathobiology, as well as human aggressive behavioral disorders and other neuropsychiatric illnesses.

Conflict of interest

None.

Acknowledgements

The research was supported by the Russian Foundation for Basic Research (RFBR) grant 16-04-00851 to AVK. KAD is supported by the RFBR grant18-34-00996, and is a recipient of the Special Rector's Fellowship for SPSU PhD Students. DBR received the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) research productivity grant 307595/2015-3. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. AVK is the Chair of the International Zebrafish Neuroscience Research Consortium (ZNRC) which coordinated this multi-lab collaborative study.

References

Abril-de-Abreu, R., Cruz, J., Oliveira, R.F., 2015. Social eavesdropping in zebrafish: tuning of attention to social interactions. Sci. Rep. 5, 12678.
Albers, H.E., 2012. The regulation of social recognition, social communication and aggression: vasopressin in the social behavior neural network. Horm. Behav. 61, 283–292.
Aliczki, M., Varga, Z.K., Balogh, Z., Haller, J., 2015. Involvement of 2-arachidonoylglycerol signaling in social challenge responding of male CD1 mice. Psychopharmacology 232, 2157–2167.
Aman, M.G., Bukstein, O.G., Gadow, K.D., Arnold, L.E., Molina, B.S.G., McNamara, N.K., Rundberg-Rivera, E.V., Li, X.B., Kipp, H., Schneider, J., Butter, E.M., Baker, J., Sprafkin, J., Rice, R.R., Bangalore, S.S., Farmer, C.A., Austin, A.B., Buchan-Page, K.A., Brown, N.V., Hurt, E.A., Grondhuis, S.N., Findling, R.L., 2014. What does risperidone add to parent training and stimulant for severe aggression in child Attention-Deficit/Hyperactivity disorder? J. Am. Acad. Child Adolesc. Psychiatry 53, 47–60.
Ariyomo, T.O., Carter, M., Watt, P.J., 2013. Heritability of boldness and aggressiveness in the zebrafish. Behav. Genet. 43, 161–167.
Ariyomo, T.O., Watt, P.J., 2013. Aggression and sex differences in lateralization in the zebrafish. Anim. Behav. 86, 617–622.
Association, A.P., 2013. Diagnostic and Statistical Manual of Mental Disorders, fifth edition. pp. 947 (DSM-V).
Balzarini, V., Taborsky, M., Wanner, S., Koch, F., Frommen, J.G., 2014. Mirror, mirror on the wall: the predictive value of mirror tests for measuring aggression in fish. Behav. Ecol. Sociobiol. 68, 871–878.
Barbazuk, W.B., Korf, I., Kadavi, C., Heyen, J., Tate, S., Wun, E., Bedell, J.A., McPherson, J.D., Johnson, S.L., 2000. The syntenic relationship of the zebrafish and human genomes. Genome Res. 10, 1351–1358.
Barlow, G.W., 1992. Is mating different in monogamous species - the Midas cichlid fish as a case-study. Am. Zool. 32, 91–99.
Beeching, S.C., 1992. Visual assessment of relative body size in a cichlid fish, the oscar, astronotus-ocellatus. Ethology 90, 177–186.
Berton, O., Hahn, C.G., Thase, M.E., 2012. Are we getting closer to valid translational models for major depression? Science 338, 75–79.
Bhat, A., Greulich, M.M., Martins, E.P., 2015. Behavioral plasticity in response to environmental manipulation among zebrafish (*Danio rerio*) populations. PLoS One 10, e0125097.
Blakely-McClure, S.J., Ostrov, J.M., 2016. Relational aggression, victimization and self-concept: testing pathways from middle childhood to adolescence. J. Youth Adolesc. 45, 376–390.
Blaser, R., Gerlai, R., 2006. Behavioral phenotyping in zebrafish: comparison of three behavioral quantification methods. Behav. Res. Methods 38, 456–469.
Bonan, C.D., Norton, W.H.J., 2015. The utility of zebrafish as a model for behavioural genetics. Curr. Opin. Behav. Sci. 2, 34–38.
Bond, A.B., 1992. Aggressive motivation in the midas cichlid - evidence for behavioral efference. Behaviour 122, 135–152.
Bridi, D., Altenhofen, S., Gonzalez, J.B., Reolon, G.K., Bonan, C.D., 2017. Glyphosate and Roundup (R) alter morphology and behavior in zebrafish. Toxicology 392, 32–39.
Brodie, M.J., Besag, F., Ettinger, A.B., Mula, M., Gobbi, G., Comai, S., Aldenkamp, A.P.,

Steinhoff, B.J., 2016. Epilepsy, antiepileptic drugs, and aggression: an evidence-based review. Pharmacol. Rev. 68, 563–602.
Burokas, A., Gutierrez-Cuesta, J., Martin-Garcia, E., Maldonado, R., 2012. Operant model of frustrated expected reward in mice. Addict. Biol. 17, 770–782.
Carreno Gutierrez, H., O'Leary, A., Freudenberg, F., Fedele, G., Wilkinson, R., Markham, E., van Eeden, F., Reif, A., Norton, W.H.J., 2017. Nitric oxide interacts with monoamine oxidase to modulate aggression and anxiety-like behaviour. Eur. Neuropsychopharmacol.
Chen, J.F., Tanguay, R.L., Simonich, M., Nie, S.F., Zhao, Y.X., Li, L.L., Bai, C.L., Dong, Q.X., Huang, C.J., Lin, K.F., 2016. TBBPA chronic exposure produces sex-specific neurobehavioral and social interaction changes in adult zebrafish. Neurotoxicol. Teratol. 56, 9–15.
Chen, P., Coccaro, E.F., Jacobson, K.C., 2012. Hostile attributional bias, negative emotional responding, and aggression in adults: moderating effects of gender and impulsivity. Aggress. Behav. 38, 47–63.
Clement, T.S., Parikh, V., Schrumpf, M., Fernald, R.D., 2005. Behavioral coping strategies in a cichlid fish: the role of social status and acute stress response in direct and displaced aggression. Horm. Behav. 47, 336–342.
Colman, J.R., Baldwin, D., Johnson, L.L., Scholz, N.L., 2009. Effects of the synthetic estrogen, 17 alpha-ethinylestradiol, on aggression and courtship behavior in male zebrafish (*Danio rerio*). Aquat. Toxicol. 91, 346–354.
Comai, S., Tau, M., Gobbi, G., 2012. The psychopharmacology of aggressive behavior: a translational approach part 1: neurobiology. J. Clin. Psychopharmacol. 32, 83–94.
Cosgrove, V.E., Kelsoe, J.R., Suppes, T., 2016. Toward a valid animal model of bipolar disorder: how the research domain criteria help bridge the clinical-basic science divide. Biol. Psychiatry 79, 62–70.
Cruz, A.S., Oliveira, R.F., 2015. Audience effects and aggressive priming in agonistic behaviour of male zebrafish, *Danio rerio*. Anim. Behav. 107, 269–276.
Dahlbom, S.J., Backstrom, T., Lundstedt-Enkel, K., Winberg, S., 2012. Aggression and monoamines: effects of sex and social rank in zebrafish (*Danio rerio*). Behav. Brain Res. 228, 333–338.
Dahlbom, S.J., Lagman, D., Lundstedt-Enkel, K., Sundstrom, L.F., Winberg, S., 2011. Boldness predicts social status in zebrafish (*Danio rerio*). PLoS One 6, e23565.
de Almeida, R.M.M., Cabral, J.C.C., Narvaes, R., 2015. Behavioural, hormonal and neurobiological mechanisms of aggressive behaviour in human and nonhuman primates. Physiol. Behav. 143, 121–135.
Echevarria, D.J., Toms, C.N., Jouandot, D.J., 2011. Alcohol-induced behavior change in zebrafish models. Rev. Neurosci. 22, 85–93.
Egan, R.J., Bergner, C.L., Hart, P.C., Cachat, J.M., Canavello, P.R., Elegante, M.F., Elkhayat, S.I., Bartels, B.K., Tien, A.K., Tien, D.H., Mohnot, S., Beeson, E., Glasgow, E., Amri, H., Zukowska, Z., Kalueff, A.V., 2009. Understanding behavioral and physiological phenotypes of stress and anxiety in zebrafish. Behav. Brain Res. 205, 38–44.
Ende, G., Cackowski, S., Van Eijk, J., Sack, M., Demirakca, T., Kleindienst, N., Bohus, M., Sobanski, E., Krause-Utz, A., Schmahl, C., 2016. Impulsivity and aggression in female BPD and ADHD patients: association with ACC glutamate and GABA concentrations. Neuropsychopharmacology 41, 410–418.
Fangmeier, M.L., Noble, D.W., O'Dea, R.E., Usui, T., Lagisz, M., Hesselson, D., Nakagawa, S., 2018. Computer animation technology in behavioral sciences: a sequential, automatic, and high-throughput approach to quantifying personality in zebrafish (*Danio rerio*). Zebrafish 15, 206–210.
Fareri, D.S., Gabard-Durnam, L., Goff, B., Flannery, J., Gee, D.G., Lumian, D.S., Caldera, C., Tottenham, N., 2017. Altered ventral striatal-medial prefrontal cortex resting-state connectivity mediates adolescent social problems after early institutional care. Dev. Psychopathol. 29, 1865–1876.
Ferrari, P.F., Palanza, P., Parmigiani, S., de Almeida, R.M.M., Miczek, K.A., 2005. Serotonin and aggressive behavior in rodents and nonhuman primates: predispositions and plasticity. Eur. J. Pharmacol. 526, 259–273.
Fetissov, S.O., Hallman, J., Nilsson, I., Lefvert, A.K., Oreland, L., Hokfelt, T., 2006. Aggressive behavior linked to corticotropin-reactive autoantibodies. Biol. Psychiatry 60, 799–802.
Filby, A.L., Paull, G.C., Hickmore, T.F.A., Tyler, C.R., 2010. Unravelling the neurophysiological basis of aggression in a fish model. BMC Genomics 11.
Filby, A.L., Paull, G.C., Searle, F., Ortiz-Zarragoitia, M., Tyler, C.R., 2012. Environmental Estrogen-Induced Alterations of Male Aggression and Dominance Hierarchies in Fish: A Mechanistic Analysis. Environ. Sci. Technol. 46, 3472–3479.
Fonagy, P., Luyten, P., 2017. Conduct problems in youth and the RDoC approach: A developmental, evolutionary-based view. Clin. Psychol. Rev.
Fontana, B.D., Meinerz, D.L., Rosa, L.V., Mezzomo, N.J., Silveira, A., Giuliani, G.S., Quadros, V.A., Filho, G.L., Blaser, R.E., Rosemberg, D.B., 2016. Modulatory action of taurine on ethanol-induced aggressive behavior in zebrafish. Pharmacol. Biochem. Behav. 141, 18–27.
Fontana, B.D., Mezzomo, N.J., Kalueff, A.V., Rosemberg, D.B., 2018. The developing utility of zebrafish models of neurological and neuropsychiatric disorders: a critical review. Exp. Neurol. 299, 157–171.
Freudenberg, F., Carreno Gutierrez, H., Post, A.M., Reif, A., Norton, W.H., 2016. Aggression in non-human vertebrates: genetic mechanisms and molecular pathways. Am. J. Med. Genet. B Neuropsychiatr. Genet. 171, 603–640.
Frigerio, C.S., De Strooper, B., 2016. Alzheimer's Disease Mechanisms and Emerging Roads to Novel Therapeutics. Annu. Rev. Neurosci. 39 (39), 57–79.
Friske, J.E., Gammie, S.C., 2005. Environmental enrichment alters plus maze, but not maternal defense performance in mice. Physiol. Behav. 85, 187–194.
Gallup Jr., G.G., 1968. Mirror-image stimulation. Psychol. Bull. 70, 782–793.
Gazquez, J.J., Perez-Fuentes, M.D., Molero, M.D., Martin, A.B.B., Martinez, A.M., Sanchez-Marchan, C., 2016. Drug use in adolescents in relation to social support and reactive and proactive aggressive behavior. Psicothema 28, 318–322.
Gerlai, R., 2003. Zebra fish: an uncharted behavior genetic model. Behav. Genet. 33, 461–468.
Gerlai, R., 2010. Zebrafish antipredatory responses: a future for translational research? Behav. Brain Res. 207, 223–231.
Gerlai, R., Lahav, M., Guo, S., Rosenthal, A., 2000. Drinks like a fish: zebra fish (*Danio rerio*) as a behavior genetic model to study alcohol effects. Pharmacol. Biochem. Behav. 67, 773–782.
Ghiselli, W.B., Thor, D.H., 1974. Rodent model of irritable aggression - method for analyses of individual roles in paired fighting. Bull. Psychon. Soc. 4, 17–19.
Giacomini, A., Abreu, M.S., Giacomini, L.V., Siebel, A.M., Zimerman, F.F., Rambo, C.L., Mocelin, R., Bonan, C.D., Piato, A.L., Barcellos, L.J.G., 2016. Fluoxetine and diazepam acutely modulate stress induced-behavior. Behav. Brain Res. 296, 301–310.
Gleason, E.D., Fuxjager, M.J., Oyegbile, T.O., Marler, C.A., 2009. Testosterone release and social context: when it occurs and why. Front. Neuroendocrinol. 30, 460–469.
Glushakov, A.V., Glushakova, O.Y., Dore, S., Carney, P.R. and Hayes, R.L. 2016. Animal Models of Posttraumatic Seizures and Epilepsy. Injury Models of the Central Nervous System: Methods and Protocols, 1462: 481-519.
Godwin, J., Thompson, R., 2012. Nonapeptides and social behavior in fishes. Horm. Behav. 61, 230–238.
Gonzalez-Gomez, P.L., Blakeslee, W.S., Razeto-Barry, P., Borthwell, R.M., Hiebert, S.M., Wingfield, J.C., 2014. Aggression, body condition, and seasonal changes in sex-steroids in four hummingbird species. J. Ornithol. 155, 1017–1025.
Green, J., Collins, C., Kyzar, E.J., Pham, M., Roth, A., Gaikwad, S., Cachat, J., Stewart, A.M., Landsman, S., Grieco, F., Tegelenbosch, R., Noldus, L.P., Kalueff, A.V., 2012. Automated high-throughput neurophenotyping of zebrafish social behavior. J. Neurosci. Methods 210, 266–271.
Haller, J., Kruk, M.R., 2006. Normal and abnormal aggression: human disorders and novel laboratory models. Neurosci. Biobehav. Rev. 30, 292–303.
Hamilton, D.A., Barto, D., Rodriguez, C.I., Magcalas, C.M., Fink, B.C., Rice, J.P., Bird, C.W., Davies, S., Savage, D.D., 2014. Effects of moderate prenatal ethanol exposure and age on social behavior, spatial response perseveration errors and motor behavior. Behav. Brain Res. 269, 44–54.
Harrington, M.E., 1995. Aggression in damselfish - habituation by adults of pomacentrus-partitus to juvenile intruders. Environ. Biol. Fishes 42, 25–35.
Herculano, A.M., Maximino, C., 2014. Serotonergic modulation of zebrafish behavior: towards a paradox. Prog. Neuropsychopharmacol. Biol. Psychiatry 55, 50–66.
Herpertz, S.C., Nagy, K., Ueltzhoffer, K., Schmitt, R., Mancke, F., Schmahl, C., Bertsch, K., 2017. Brain mechanisms underlying reactive aggression in borderline personality disorder-sex matters. Biol. Psychiatry 82, 257–266.
Hirschenhauser, K., Oliveira, R.F., 2006. Social modulation of androgens in male vertebrates: meta-analyses of the challenge hypothesis. Anim. Behav. 71, 265–277.
Holekamp, K.E., Strauss, E.D., 2016. Aggression and dominance: an interdisciplinary overview. Curr. Opin. Behav. Sci. 12, 44–51.
Hoptman, M.J., 2015. Impulsivity and aggression in schizophrenia: a neural circuitry perspective with implications for treatment. CNS Spectr. 20, 280–286.
Hortopan, G.A., Dinday, M.T., Baraban, S.C., 2010. Zebrafish as a model for studying genetic aspects of epilepsy. Dis. Model. Mech. 3, 144–148.
Howe, K., Clark, M.D., Torroja, C.F., Torrance, J., Berthelot, C., Muffato, M., Collins, J.E., Humphray, S., McLaren, K., Matthews, L., McLaren, S., Sealy, I., Caccamo, M., Churcher, C., Scott, C., Barrett, J.C., Koch, R., Rauch, G.J., White, S., Chow, W., Kilian, B., Quintais, L.T., Guerra-Assuncao, J.A., Zhou, Y., Gu, Y., Yen, J., Vogel, J.H., Eyre, T., Redmond, S., Banerjee, R., Chi, J., Fu, B., Langley, E., Maguire, S.F., Laird, G.K., Lloyd, D., Kenyon, E., Donaldson, S., Sehra, H., Almeida-King, J., Loveland, J., Trevanion, S., Jones, M., Quail, M., Willey, D., Hunt, A., Burton, J., Sims, S., McLay, K., Plumb, B., Davis, J., Clee, C., Oliver, K., Clark, R., Riddle, C., Elliot, D., Threadgold, G., Harden, G., Ware, D., Begum, S., Mortimore, B., Kerry, G., Heath, P., Phillimore, B., Tracey, A., Corby, N., Dunn, M., Johnson, C., Wood, J., Clark, S., Pelan, S., Griffiths, G., Smith, M., Glithero, R., Howden, P., Barker, N., Lloyd, C., Stevens, C., Harley, J., Holt, K., Panagiotidis, G., Lovell, J., Beasley, H., Henderson, C., Gordon, D., Auger, K., Wright, D., Collins, J., Raisen, C., Dyer, L., Leung, K., Robertson, L., Ambridge, K., Leongamornlert, D., McGuire, S., Gilderthorp, R., Griffiths, C., Manthravadi, D., Nichol, S., Barker, G., Whitehead, S., Kay, M., Brown, J., Murnane, C., Gray, E., Humphries, M., Sycamore, N., Barker, D., Saunders, D., Wallis, J., Babbage, A., Hammond, S., Mashreghi-Mohammadi, M., Barr, L., Martin, S., Wray, P., Ellington, A., Matthews, N., Ellwood, M., Woodmansey, R., Clark, G., Cooper, J., Tromans, A., Grafham, D., Skuce, C., Pandian, R., Andrews, R., Harrison, E., Kimberley, A., Garnett, J., Fosker, N., Hall, R., Garner, P., Kelly, D., Bird, C., Palmer, S., Gehring, I., Berger, A., Dooley, C.M., Ersan-Urun, Z., Eser, C., Geiger, H., Geisler, M., Karotki, L., Kirn, A., Konantz, J., Konantz, M., Oberlander, M., Rudolph-Geiger, S., Teucke, M., Lanz, C., Raddatz, G., Osoegawa, K., Zhu, B., Rapp, A., Widaa, S., Langford, C., Yang, F., Schuster, S.C., Carter, N.P., Harrow, J., Ning, Z., Herrero, J., Searle, S.M., Enright, A., Geisler, R., Plasterk, R.H., Lee, C., Westerfield, M., de Jong, P.J., Zon, L.I., Postlethwait, J.H., Nusslein-Volhard, C., Hubbard, T.J., Roest Crollius, H., Rogers, J., Stemple, D.L., 2013. The zebrafish reference genome sequence and its relationship to the human genome. Nature 496, 498–503.
Ilchibaeva, T.V., Tsybko, A.S., Kozhemyakina, R.V., Konoshenko, M.Y., Popova, N.K., Naumenko, V.S., 2017. The relationship between different types of genetically defined aggressive behavior. J. Ethol. 35, 75–81.
Jantzen, C.E., Annunziato, K.M., Cooper, K.R., 2016. Behavioral, morphometric, and gene expression effects in adult zebrafish (*Danio rerio*) embryonically exposed to PFOA, PFOS, and PFNA. Aquat. Toxicol. 180, 123–130.
Jha, P., 2010. Comparative study of aggressive behaviour in transgenic and wildtype zebrafish Danio rerio (Hamilton) and the flying barb Esomus danricus (Hamilton), and their susceptibility to predation by the snakehead *Channa striatus (Bloch)*. Ital. J. Zool. (Modena) 77, 102–109.
Jones, L.J., Norton, W.H., 2015. Using zebrafish to uncover the genetic and neural basis of

aggression, a frequent comorbid symptom of psychiatric disorders. Behav. Brain Res. 276, 171–180.
Kalueff, A.V., Gebhardt, M., Stewart, A.M., Cachat, J.M., Brimmer, M., Chawla, J.S., Craddock, C., Kyzar, E.J., Roth, A., Landsman, S., Gaikwad, S., Robinson, K., Baatrup, E., Tierney, K., Shamchuk, A., Norton, W., Miller, N., Nicolson, T., Braubach, O., Gilman, C.P., Pittman, J., Rosemberg, D.B., Gerlai, R., Echevarria, D., Lamb, E., Neuhauss, S.C., Weng, W., Bally-Cuif, L., Schneider, H., Zebrafish Neuroscience Research, C, 2013. Towards a comprehensive catalog of zebrafish behavior 1.0 and beyond. Zebrafish 10, 70–86.
Kalueff, A.V., Ren-Patterson, R.F., LaPorte, J.L., Murphy, D.L., 2008. Domain interplay concept in animal models of neuropsychiatric disorders: a new strategy for high-throughput neurophenotyping research. Behav. Brain Res. 188, 243–249.
Kalueff, A.V., Stewart, A.M., Gerlai, R., 2014. Zebrafish as an emerging model for studying complex brain disorders. Trends Pharmacol. Sci. 35, 63–75.
Kalueff, A.V., Stewart, A.M., Song, C., Gottesman, I.I., 2015. Targeting dynamic interplay among disordered domains or endophenotypes to understand complex neuropsychiatric disorders: translational lessons from preclinical models. Neurosci. Biobehav. Rev. 53, 25–36.
Kawai, K., Nozaki, T., Nishikata, H., Aou, S., Takii, M., Kubo, C., 2003. Aggressive behavior and serum testosterone concentration during the maturation process of male mice: the effects of fetal exposure to bisphenol A. Environ. Health Perspect. 111, 175–178.
Kelly, J.R., Clarke, G., Cryan, J.F., Dinan, T.G., 2018. Dimensional thinking in psychiatry in the era of the Research Domain Criteria (RDoC). Ir. J. Psychol. Med. 35, 89–94.
Kiss, J.P., 2000. Role of nitric oxide in the regulation of monoaminergic neurotransmission. Brain Res. Bull. 52, 459–466.
Kovalenko, I.L., Galyamina, A.G., Smagin, D.A., Michurina, T.V., Kudryavtseva, N.N., Enikolopov, G., 2014. Extended effect of chronic social defeat stress in childhood on behaviors in adulthood. PLoS One 9.
Krug 2nd, R.G., Lee, H.B., El Khoury, L.Y., Sigafoos, A.N., Petersen, M.O., Clark, K.J., 2018. The endocannabinoid gene faah2a modulates stress-associated behavior in zebrafish. PLoS One 13, e0190897.
Kudryavtseva, N.N., Smagin, D.A., Kovalenko, I.L., Galyamina, A.G., Vishnivetskaya, G.B., Babenko, V.N., Orlov, Y.L., 2017. Serotonergic genes in the development of anxiety/depression-like state and pathology of aggressive behavior in male mice: RNA-seq data. Mol. Biol. (Mosk) 51, 288–300.
Kudryavtseva, N.N., Smagin, D.A., Kovalenko, I.L., Vishnivetskaya, G.B., 2014. Repeated positive fighting experience in male inbred mice. Nat. Protoc. 9, 2705–2717.
Kyzar, E.J., Collins, C., Gaikwad, S., Green, J., Roth, A., Monnig, L., El-Ounsi, M., Davis, A., Freeman, A., Capezio, N., Stewart, A.M., Kalueff, A.V., 2012. Effects of hallucinogenic agents mescaline and phencyclidine on zebrafish behavior and physiology. Prog. Neuropsychopharmacol. Biol. Psychiatry 37, 194–202.
LaPorte, J.L., Egan, R.J., Hart, P.C., Bergner, C.L., Cachat, J.M., Canavello, P.R., Kalueff, A.V., 2010. Qui non proficit, deficit: experimental models for' integrative' research of affective disorders. J. Affect. Disord. 121, 1–9.
Larson, E.T., O'Malley, D.M., Melloni, R.H., 2006. Aggression and vasotocin are associated with dominant-subordinate relationships in zebrafish. Behav. Brain Res. 167, 94–102.
Leibenluft, E., 2017. Pediatric irritability: a systems neuroscience approach. Trends Cogn. Sci. 21, 277–289.
Leibenluft, E., Stoddard, J., 2013. The developmental psychopathology of irritability. Dev. Psychopathol. 25, 1473–1487.
Lieschke, G.J., Currie, P.D., 2007. Animal models of human disease: zebrafish swim into view. Nat. Rev. Genet. 8, 353–367.
Lindeyer, C.M., Langen, E.M.A., Swaney, W.T., Reader, S.M., 2015. Nonapeptide influences on social behaviour: effects of vasotocin and isotocin on shoaling and interaction in zebrafish. Behaviour 152, 897–915.
Liu, J.T., Zhong, R., Xiong, W., Liu, H.B., Eisenegger, C., Zhou, X.L., 2017. Melatonin increases reactive aggression in humans. Psychopharmacology 234, 2971–2978.
Lobbestael, J., Cima, M., Arntz, A., 2013. The relationship between adult reactive and proactive aggression, hostile interpretation bias, and antisocial personality disorder. J. Pers. Disord. 27, 53–66.
Lopes, J.S., Abril-de-Abreu, R., Oliveira, R.F., 2015. Brain transcriptomic response to social eavesdropping in zebrafish (*Danio rerio*). PLoS One 10, e0145801.
Lopez, J.M., Moreno, N., Morona, R., Munoz, M., Gonzalez, A., 2005. Colocalization of nitric oxide synthase and monoamines in neurons of the amphibian brain. Brain Res. Bull. 66, 555–559.
Louise von Borries, A.K., Volman, I., de Bruijn, E.R., Bulten, B.H., Verkes, R.J., Roelofs, K., 2012. Psychopaths lack the automatic avoidance of social threat: relation to instrumental aggression. Psychiatry Res. 200, 761–766.
Lu, Y.F., Menard, S., 2017. The interplay of MAOA and peer influences in predicting adult criminal behavior. Psychiatr. Q. 88, 115–128.
Lumley, L.A., Charles, R.F., Charles, R.C., Hebert, M.A., Morton, D.M., Meyerhoff, J.L., 2000. Effects of social defeat and of diazepam on behavior in a resident-intruder test in male DBA/2 mice. Pharmacol. Biochem. Behav. 67, 433–447.
Madeira, N., Oliveira, R.F., 2017. Long-term social recognition memory in Zebrafish. Zebrafish 14, 305–310.
Malki, K., Du Rietz, E., Crusio, W.E., Pain, O., Paya-Cano, J., Karadaghi, R.L., Sluyter, F., de Boer, S.F., Sandnabba, K., Schalkwyk, L.C., Asherson, P., Tosto, M.G., 2016. Transcriptome analysis of genes and gene networks involved in aggressive behavior in mouse and zebrafish. Am. J. Med. Genet. B Neuropsychiatr. Genet. 171, 827–838.
Marquez-Arias, A., Santillan-Doherty, A.M., Arenas-Rosas, R.V., Gasca-Matias, M.P., Munoz-Delgado, J., 2010. Environmental enrichment for captive stumptail macaques (*Macaca arctoides*). J. Med. Primatol. 39, 32–40.
Martins, E.P., Bhat, A., 2014. Population-level personalities in zebrafish: aggression-boldness across but not within populations. Behav. Ecol. 25, 368–373.
Mazur, A., Booth, A., 1998. Testosterone and dominance in men. Behav. Brain Sci. 21, 353.
McCammon, J.M., Sive, H., 2015. Addressing the genetics of human mental health disorders in model organisms. Annu. Rev. Genomics Hum. Genet. 16, 173–197.
McGonigle, P., 2014. Animal models of CNS disorders. Biochem. Pharmacol. 87, 140–149.
McLaughlin, K.A., Green, J.G., Hwang, I., Sampson, N.A., Zaslavsky, A.M., Kessler, R.C., 2012. Intermittent explosive disorder in the national comorbidity survey replication adolescent supplement. Arch. Gen. Psychiatry 69, 1131–1139.
McPartland, J.M., Glass, M., Matias, I., Norris, R.W., Kilpatrick, C.W., 2007. A shifted repertoire of endocannabinoid genes in the zebrafish (*Danio rerio*). Mol. Genet. Genom. 277, 555–570.
Mechoulam, R., 2002. Discovery of endocannabinoids and some random thoughts on their possible roles in neuroprotection and aggression. Prostaglandins Leukot. Essent. Fatty Acids 66, 93–99.
Michelotti, P., Quadros, V.A., Pereira, M.E., Rosemberg, D.B., 2018. Ketamine modulates aggressive behavior in adult zebrafish. Neurosci. Lett. 684, 164–168.
Miczek, K.A., Faccidomo, S., De Almeida, R.M., Bannai, M., Fish, E.W., Debold, J.F., 2004. Escalated aggressive behavior: new pharmacotherapeutic approaches and opportunities. Ann. N. Y. Acad. Sci. 1036, 336–355.
Mutlu, O., Ulak, G., Laugeray, A., Belzung, C., 2009. Effects of neuronal and inducible NOS inhibitor 1-[2-(trifluoromethyl) phenyl] imidazole (TRIM) in unpredictable chronic mild stress procedure in mice. Pharmacol. Biochem. Behav. 92, 82–87.
Nabinger, D.D., Altenhofen, S., Bitencourt, P.E.R., Nery, L.R., Leite, C.E., Vianna, M., Bonan, C.D., 2017. Nickel exposure alters behavioral parameters in larval and adult zebrafish. Sci. Total Environ.
Naumenko, V.S., Kozhemyakina, R.V., Plyusnina, I.F., Kulikov, A.V., Popova, N.K., 2013. Serotonin 5-HT1A receptor in infancy-onset aggression: comparison with genetically defined aggression in adult rats. Behav. Brain Res. 243, 97–101.
Nelson, R.J., Trainor, B.C., 2007. Neural mechanisms of aggression. Nat. Rev. Neurosci. 8, 536–546.
Nguyen, M., Poudel, M.K., Stewart, A.M., Kalueff, A.V., 2013a. Skin too thin? The developing utility of zebrafish skin (neuro)pharmacology for CNS drug discovery research. Brain Res. Bull. 98, 145–154.
Nguyen, M., Yang, E., Neelkantan, N., Mikhaylova, A., Arnold, R., Poudel, M.K., Stewart, A.M., Kalueff, A.V., 2013b. Developing 'integrative' zebrafish models of behavioral and metabolic disorders. Behav. Brain Res. 256, 172–187.
Norton, W., Bally-Cuif, L., 2010. Adult zebrafish as a model organism for behavioural genetics. BMC Neurosci. 11.
Norton, W.H.J., Stumpenhorst, K., Faus-Kessler, T., Folchert, A., Rohner, N., Harris, M.P., Callebert, J., Bally-Cuif, L., 2011. Modulation of Fgfr1a signaling in zebrafish reveals a genetic basis for the aggression-boldness syndrome. J. Neurosci. 31, 13796–13807.
Nunes, A.R., Ruhl, N., Winberg, S., Oliveira, R.F., 2017a. Social phenotypes in zebrafish. In: Kalueff, A.V. (Ed.), The Rights and Wrongs of Zebrafish: Behavioral Phenotyping of Zebrafish.
Nunes, M.E., Muller, T.E., Braga, M.M., Fontana, B.D., Quadros, V.A., Marins, A., Rodrigues, C., Menezes, C., Rosemberg, D.B., Loro, V.L., 2017b. Chronic treatment with paraquat induces brain injury, changes in antioxidant defenses system, and modulates behavioral functions in zebrafish. Mol. Neurobiol. 54, 3925–3934.
Oliveira, R.F., McGregor, P.K., Latruffe, C., 1998. Know thine enemy: fighting fish gather information from observing conspecific interactions. Proc. R. Soc. Lond. B Biol. Sci. 265, 1045–1049.
Oliveira, R.F., Silva, J.F., Simoes, J.M., 2011. Fighting zebrafish: characterization of aggressive behavior and winner-loser effects. Zebrafish 8, 73–81.
Oliveira, R.F., Simoes, J.M., Teles, M.C., Oliveira, C.R., Becker, J.D., Lopes, J.S., 2016. Assessment of fight outcome is needed to activate socially driven transcriptional changes in the zebrafish brain. Proc. Natl. Acad. Sci. U. S. A. 113, E654–61.
Olivier, B., Mos, J., vanOorschot, R., Hen, R., 1995. Serotonin receptors and animal models of aggressive behavior. Pharmacopsychiatry 28, 80–90.
Overli, O., Korzan, W.J., Hoglund, E., Winberg, S., Bollig, H., Watt, M., Forster, G.L., Barton, B.A., Overli, E., Renner, K.J., Summers, C.H., 2004. Stress coping style predicts aggression and social dominance in rainbow trout. Horm. Behav. 45, 235–241.
Palanza, P., Parmigiani, S., 2017. How does sex matter? Behavior, stress and animal models of neurobehavioral disorders. Neurosci. Biobehav. Rev. 76, 134–143.
Pardon, M.C., Gerardin, P., Joubert, C., Perez-Diaz, F., Cohen-Salmon, C., 2000. Influence of prepartum chronic ultramild stress on maternal pup care behavior in mice. Biol. Psychiatry 47, 858–863.
Park, C., Clements, K.N., Issa, F.A., Ahn, S., 2018. Effects of social experience on the habituation rate of zebrafish startle escape response: empirical and computational analyses. Front. Neural Circuits 12.
Parker, M.O., Annan, L.V., Kanellopoulos, A.H., Brock, A.J., Combe, F.J., Baiamonte, M., Teh, M.T., Brennan, C.H., 2014. The utility of zebrafish to study the mechanisms by which ethanol affects social behavior and anxiety during early brain development. Prog. Neuropsychopharmacol. Biol. Psychiatry 55, 94–100.
Patki, G., Atrooz, F., Alkadhi, I., Solanki, N., Salim, S., 2015. High aggression in rats is associated with elevated stress, anxiety-like behavior, and altered catecholamine content in the brain. Neurosci. Lett. 584, 308–313.
Paull, G.C., Filby, A.L., Giddins, H.G., Coe, T.S., Hamilton, P.B., Tyler, C.R., 2010. Dominance hierarchies in zebrafish (*Danio rerio*) and their relationship with reproductive success. Zebrafish 7, 109–117.
Pavlidis, M., Sundvik, M., Chen, Y.C., Panula, P., 2011. Adaptive changes in zebrafish brain in dominant-subordinate behavioral context. Behav. Brain Res. 225, 529–537.
Peper, J.S., de Reus, M.A., van den Heuvel, M.P., Schutter, D.J.L.G., 2015. Short Fused? Associations between white matter connections, sex steroids, and aggression across adolescence. Hum. Brain Mapp. 36, 1043–1052.
Pogoda, H.M., Hammerschmidt, M., 2007. Molecular genetics of pituitary development in zebrafish. Semin. Cell Dev. Biol. 18, 543–558.

Price, A.C., Weadick, C.J., Shim, J., Rodd, F.H., 2008. Pigments, patterns, and fish behavior. Zebrafish 5, 297–307.
Provencal, N., Booij, L., Tremblay, R.E., 2015. The developmental origins of chronic physical aggression: biological pathways triggered by early life adversity. J. Exp. Biol. 218, 123–133.
Qouta, S., Punamaki, R.L., Miller, T., El-Sarraj, E., 2008. Does war beget child aggression? Military violence, gender, age and aggressive behavior in two Palestinian samples. Aggress. Behav. 34, 231–244.
Quadros, I.M., Hwa, L.S., Shimamoto, A., Carlson, J., DeBold, J.F., Miczek, K.A., 2014. Prevention of alcohol-heightened aggression by CRF-RI antagonists in mice: critical role for DRN-PFC serotonin pathway. Neuropsychopharmacology 39, 2874–2883.
Ramallo, M.R., Birba, A., Honji, R.M., Morandini, L., Moreira, R.G., Somoza, G.M., Pandolfi, M., 2015. A multidisciplinary study on social status and the relationship between inter-individual variation in hormone levels and agonistic behavior in a Neotropical cichlid fish. Horm. Behav. 69, 139–151.
Rambo, C.L., Mocelin, R., Marcon, M., Villanova, D., Koakoski, G., de Abreu, M.S., Oliveira, T.A., Barcellos, L.J.G., Piato, A.L., Bonan, C.D., 2017. Gender differences in aggression and cortisol levels in zebrafish subjected to unpredictable chronic stress. Physiol. Behav. 171, 50–54.
Reolon, G.K., de Melo, G.M., da Rosa, J.G.D., Barcellos, L.J.G., Bonan, C.D., 2018. Sex and the housing: effects on behavior, cortisol levels and weight in zebrafish. Behav. Brain Res. 336, 85–92.
Repple, J., Pawliczek, C.M., Voss, B., Siegel, S., Schneider, F., Kohn, N., Habel, U., 2017. From provocation to aggression: the neural network. BMC Neurosci. 18, 73.
Rey, S., Digka, N., MacKenzie, S., 2015. Animal personality relates to thermal preference in wild-type zebrafish, Danio rerio. Zebrafish 12, 243–249.
Ricci, L., Summers, C.H., Larson, E.T., O'Malley, D., Melloni, R.H., 2013. Development of aggressive phenotypes in zebrafish: interactions of age, experience and social status. Anim. Behav. 86, 245–252.
Rinkwitz, S., Mourrain, P., Becker, T.S., 2011. Zebrafish: an integrative system for neurogenomics and neurosciences. Prog. Neurobiol. 93, 231–243.
Rohner, N., Bercsenyi, M., Orban, L., Kolanczyk, M.E., Linke, D., Brand, M., Nusslein-Volhard, C., Harris, M.P., 2009. Duplication of fgfr1 permits Fgf signaling to serve as a target for selection during domestication. Curr. Biol. 19, 1642–1647.
Rosell, D.R., Siever, L.J., 2015. The neurobiology of aggression and violence. CNS Spectr. 20, 254–279.
Rosenfeld, C.S., 2015. Bisphenol A and phthalate endocrine disruption of parental and social behaviors. Front. Neurosci. 9.
Schwartzer, J.J., Morrison, R.L., Ricci, L.A., Melloni, R.H., 2009. Paliperidone suppresses the development of the aggressive phenotype in a developmentally sensitive animal model of escalated aggression. Psychopharmacology 203, 653–663.
Seguin, J.R., Arseneault, L., Boulerice, B., Harden, P.W., Tremblay, R.E., 2002. Response perseveration in adolescent boys with stable and unstable histories of physical aggression: the role of underlying processes. J. Child Psychol. Psychiatry 43, 481–494.
Sherwin, C.M., Lewis, P.D., Perry, G.C., 1999. Effects of environmental enrichment, fluorescent and intermittent lighting on injurious pecking amongst male turkey poults. Br. Poult. Sci. 40, 592–598.
Smith, J.P., Prince, M.A., Achua, J.K., Robertson, J.M., Anderson, R.T., Ronan, P.J., Summers, C.H., 2016. Intensity of anxiety is modified via complex integrative stress circuitries. Psychoneuroendocrinology 63, 351–361.
Sneddon, L.U., Schmidt, R., Fang, Y.X., Cossins, A.R., 2011. Molecular Correlates of Social Dominance: A Novel Role for Ependymin in Aggression. PLoS One 6.
Sterling, M.E., Karatayev, O., Chang, G.Q., Algava, D.B., Leibowitz, S.F., 2015. Model of voluntary ethanol intake in zebrafish: Effect on behavior and hypothalamic orexigenic peptides. Behav. Brain Res. 278, 29–39.
Stewart, A.M., Kalueff, A.V., 2015. Developing better and more valid animal models of brain disorders. Behav. Brain Res. 276, 28–31.
Sukhodolsky, D.G., Vander Wyk, B.C., Eilbott, J.A., McCauley, S.A., Ibrahim, K., Crowley, M.J., Pelphrey, K.A., 2016. Neural mechanisms of cognitive-behavioral therapy for aggression in children and adolescents: Design of a randomized controlled trial within the National Institute for Mental Health Research Domain Criteria construct of frustrative non-reward. J. Child Adolesc. Psychopharmacol. 26, 38–48.
Suzuki, H., Lucas, L.R., 2015. Neurochemical correlates of accumbal dopamine D2 and amygdaloid 5-HT 1B receptor densities on observational learning of aggression. Cogn. Affect. Behav. Neurosci. 15, 460–474.
Teles, M.C., Dahlbom, S.J., Winberg, S., Oliveira, R.F., 2013. Social modulation of brain monoamine levels in zebrafish. Behav. Brain Res. 253, 17–24.
Teles, M.C., Oliveira, R.F., 2016a. Androgen response to social competition in a shoaling fish. Horm. Behav. 78, 8–12.
Teles, M.C., Oliveira, R.F., 2016b. Quantifying aggressive behavior in zebrafish. Methods Mol. Biol. 1451, 293–305.
Terranova, J.I., Ferris, C.F., Albers, H.E., 2017. Sex differences in the regulation of offensive aggression and dominance by arginine-vasopressin. Front. Endocrinol. 8.
Tessmar-Raible, K., Raible, F., Christodoulou, F., Guy, K., Rembold, M., Hausen, H., Arendt, D., 2007. Conserved sensory-neurosecretory cell types in annelid and fish forebrain: insights into hypothalamus evolution. Cell 129, 1389–1400.
Theodoridi, A., Tsalafouta, A., Pavlidis, M., 2017. Acute exposure to fluoxetine alters aggressive behavior of zebrafish and expression of genes involved in serotonergic system regulation. Front. Neurosci. 11, 223.
Tremblay, R.E., 2008. Understanding development and prevention of chronic physical aggression: towards experimental epigenetic studies. Philos. Trans. R. Soc. B-Biol. Sci. 363, 2613–2622.
Uchida, N., Egashira, N., Iwasaki, K., Ishibashi, A., Tashiro, R., Nogami, A., Manome, N., Abe, M., Takasaki, K., Mishima, K., Takata, J., Oishi, R., Nishimura, R., Fujiwara, M., 2009. Yokukansan inhibits social isolation-induced aggression and methamphetamine-induced hyperlocomotion in rodents. Biol. Pharm. Bull. 32, 372–375.
Umathe, S.N., Bhutada, P.S., Jain, N.S., Mundhada, Y.R., Borkar, S.S., Dhumal, B., 2009. Role of nitric oxide in obsessive-compulsive behavior and its involvement in the anti-compulsive effect of paroxetine in mice. Nitric Oxide-Biol. Chem. 21, 140–147.
Umukoro, S., Aladeokin, A.C., Eduviere, A.T., 2013. Aggressive behavior: a comprehensive review of its neurochemical mechanisms and management. Aggress. Violent Behav. 18, 195–203.
van Goozen, S.H.M., Langley, K., Northover, C., Hubble, K., Rubia, K., Schepman, K., O'Donovan, M.C., Thapar, A., 2016. Identifying mechanisms that underlie links between COMT genotype and aggression in male adolescents with ADHD. J. Child Psychol. Psychiatry 57, 472–480.
Van Loo, P.L., Van Zutphen, L.F., Baumans, V., 2003. Male management: coping with aggression problems in male laboratory mice. Lab Anim. 37, 300–313.
Vassos, E., Collier, D.A., Fazel, S., 2014. Systematic meta-analyses and field synopsis of genetic association studies of violence and aggression. Mol. Psychiatry 19, 471–477.
Veenema, A.H., 2009. Early life stress, the development of aggression and neuroendocrine and neurobiological correlates: what can we learn from animal models? Front. Neuroendocrinol. 30, 497–518.
Verona, E., Bresin, K., 2015. Aggression proneness: Transdiagnostic processes involving negative valence and cognitive systems. Int. J. Psychophysiol. 98, 321–329.
Veroude, K., Zhang-James, Y., Fernandez-Castillo, N., Bakker, M.J., Cormand, B., Faraone, S.V., 2016. Genetics of aggressive behavior: an overview. Am. J. Med. Genet. B Neuropsychiatr. Genet. 171B, 3–43.
Volicer, L., Citrome, L., Volavka, J., 2017. Measurement of agitation and aggression in adult and aged neuropsychiatric patients: review of definitions and frequently used measurement scales. CNS Spectr. 22, 407–414.
Vullioud, P., Bshary, R., Ros, A.F.H., 2013. Intra- and interspecific aggression do not modulate androgen levels in dusky gregories, yet male aggression is reduced by an androgen blocker. Horm. Behav. 64, 430–438.
Waltes, R., Chiocchetti, A.G., Freitag, C.M., 2016. The neurobiological basis of human aggression: a review on genetic and epigenetic mechanisms. Am. J. Med. Genet. B. Neuropsychiatr. Genet. 171, 650–675.
Wang, J., Wang, X., Xiong, C., Liu, J., Hu, B., Zheng, L., 2015. Chronic bisphenol A exposure alters behaviors of zebrafish (*Danio rerio*). Environ. Pollut. 206, 275–281.
Wang, Y., He, Z., Zhao, C., Li, L., 2013. Medial amygdala lesions modify aggressive behavior and immediate early gene expression in oxytocin and vasopressin neurons during intermale exposure. Behav. Brain Res. 245, 42–49.
Way, G.P., Kiesel, A.L., Ruhl, N., Snekser, J.L., McRobert, S.P., 2015. Sex differences in a shoaling-boldness behavioral syndrome, but no link with aggression. Behav. Processes 113, 7–12.
Way, G.P., Southwell, M., McRobert, S.P., 2016. Boldness, aggression, and shoaling assays for zebrafish behavioral syndromes. J. Vis. Exp.
Wilkes, L., Owen, S.F., Readman, G.D., Sloman, K.A., Wilson, R.W., 2012. Does structural enrichment for toxicology studies improve zebrafish welfare? Appl. Anim. Behav. Sci. 139, 143–150.
Wright, D., Rimmer, L.B., Pritchard, V.L., Krause, J., Butlin, R.K., 2003. Inter and intra-population variation in shoaling and boldness in the zebrafish (*Danio rerio*). Naturwissenschaften 90, 374–377.
Yang, Y.L., Joshi, S.H., Jahanshad, N., Thompson, P.M., Baker, L.A., 2017. Neural correlates of proactive and reactive aggression in adolescent twins. Aggress. Behav. 43, 230–240.
Yuan, M., Chen, Y., Huang, Y., Lu, W., 2018. Behavioral and metabolic phenotype indicate personality in zebrafish (*Danio rerio*). Front. Physiol. 9, 653.
Zhang-James, Y., Faraone, S.V., 2016. Genetic architecture for human aggression: a study of gene-phenotype relationship in OMIM. Am. J. Med. Genet. B Neuropsychiatr. Genet. 171, 641–649.
Zhu, W., Volkow, N.D., Ma, Y.M., Fowler, J.S., Wang, G.J., 2004. Relationship between ethanol-induced changes in brain regional metabolism and its motor, behavioural and cognitive effects. Alcohol Alcohol. 39, 53–58.
Zimmermann, F.F., Gaspary, K.V., Siebel, A.M., Bonan, C.D., 2016. Oxytocin reversed MK-801-induced social interaction and aggression deficits in zebrafish. Behav. Brain Res. 311, 368–374.