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Guest Editorial

Teleosts: Simple Organisms? Complex Behavior

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THE ULTIMATE OUTPUT of organismal development and maturation is behavior, and through the coming of age of the zebrafish as a large-scale genetic and genomic model organism, it is perhaps not surprising that growing attention is currently given to zebrafish as a potential model for behavioral studies as well. This has motivated the choice for this theme issue. We are hoping that the collection of reviews presented here will both provide the reader with up-to-date information on the status of zebrafish as a behavioral model, and stimulate interest for this growing research field.

The choice of topics for this issue followed several motivations.

The first was perhaps, in our zebrafish-centrist world, to rehabilitate other teleost models that have pioneered or led specific aspects of behavioral research for decades. Because fish are clearly the most diverse vertebrate phyla, with more than 20,000 species worldwide for teleosts only, they offer a remarkable variety of natural habits and phylogenetic adaptations. These have long been used and compared to study behaviors such as feeding habits, integration of environmental cues, or social interactions. Two reviews in this issue report on ethological studies of feeding behavior (Volkoff and Peter) and shoaling habits (Wright et al.) in a variety of teleosts, monitoring general patterns and species-specific variations. But the use of nonzebrafish teleosts is far from limited to the study of innate behaviors. For instance, the goldfish, for its relatively large and stereotactically well-characterized brain, has been successfully used to approach cognitive processes in teleosts. The review by Salas et al. summarizes current knowledge on a selection of learning and memory behaviors. Paradigms assessing learning/memory processes in zebrafish have also been developed.[1–3]

Our second motivation was to touch upon a variety of behaviors, whether innate or acquired, whether mostly motor responses or involving "higher" brain functions. It was long believed that teleost fish, at the bottom of the vertebrate evolutionary scale, only display a limited range and extreme simplicity of behaviors. It is our hope to straighten this view here by providing a representative overview of the repertoire of behaviors that can be studied in teleosts. In addition to those mentioned above, we also cover here in zebrafish innate behaviors such as locomotion movements (Saint-Amant), vision (Fleisch and Neuhauss), olfaction (Whitlock), and sleep (Zhdanova), as well as a range of social behaviors including predator inspection, prey recognition, innate preferences or avoidances for individuals or environmental cues (Miklósi and Andrew), and brain functions involving aminergic systems (Panula et al.). Obviously not all topics could be covered in this issue, and the reader is referred to original publications on aspects such as acoustic communication,[4–6] behavioral rhythmicity,[7–9] aggression and social dominance,[10–13] or for an increasing number of studies using the zebrafish as a model to mimic human behavioral

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disorders or to assess the developmental and behavioral effects of neurotoxins.[2,3,14–20]

"Natural" behaviors can often be modified by associative conditioning, highlighting the fine balance between innate and acquired activities, and raising caution in all behavioral studies performed on animals outside their normal environment. This leads to our third motivation, crucial in the relatively young field of zebrafish behavior: to stress the potential pitfalls of some experimental approaches (e.g., when animals are placed in artificial conditions of stress, or in social isolation), the appropriate controls to perform, and the need for balanced interpretations of behavioral "normality" or "abnormality" since laboratory conditions, whether through inbreeding or through artificial protection, likely affect natural behavior. Most authors therefore have included technical considerations, and the reviews by Wright et al. and Miklosi and Andrew especially discuss this issue.

To date, a number of behavioral paradigms are being studied in teleosts, and a major challenge now will be to establish the connection between these behaviors and the neuronal circuits and transmitters that form their mechanistic basis. For this reason, most reviews here also summarize current knowledge on associated neuronal circuitries and, when understood, their construction during development or CNS maturation. Strikingly, this circuitry and the pharmacology involved appear often comparable to those operating to control similar behaviors in higher vertebrates. This observation makes teleosts valid models for an approach to many behaviors, with the additional hope that their simpler brain organization (in particular regarding forebrain anatomy) will permit to reveal the neuronal bases underlying these functions. Likely, this understanding will also gain from the remarkable amenability of zebrafish to neuroimaging approaches, which can help reveal not only the organization of a circuitry but also its activation in response to natural or acquired behavioral tasks. Beautiful examples of such achievement have been recently published.[21–23] These will provide an unprecedented resolution towards understanding the genetic control of behavior.

Together, we are approaching a stage where teleosts, in particular zebrafish with its powerful genomics, will permit studying the interaction between genes, behavior, and the neural and endocrine processes linking these events. It makes it all the more important to define neuroanatomical and behavioral bases in these species, and we hope that this issue will also help in this crucial task.

I wish to end by acknowledging the main actors in this enterprise. I am grateful to all authors for their remarkable work. Far from being limited to a review of the published literature, it includes sharing their thoughts, experience and results on many practical and theoretical aspects of behavioral studies. I am also greatly indebted to our referees, who not only constructively improved everyone's work, but also contributed to the coherence of this issue as a whole.

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REFERENCES

1. Colwill RM, Raymond MP, Ferreira L, Escudero H. Visual discrimination learning in zebrafish (*Danio rerio*). Behav Proc 2005;70:19–31.
2. Darland T, Dowling JE. Behavioral screening for cocaine sensitivity in mutagenized zebrafish. Proc Natl Acad Sci USA 2001;98:11691–11696.
3. Ninkovic J, Folchert A, Makhankov YV, Neuhauss SC, Sillaber I, Straehle U, et al. Genetic identification of AChE as a positive modulator of addiction to the psychostimulant D-amphetamine in zebrafish. J Neurobiol 2006;66:463–475.
4. Bass AH, McKibben JR. Neural mechanisms and behaviors for acoustic communication in teleost fish. Prog Neurobiol 2003;69:1–26.
5. Ladich F. Acoustic communication and the evolution of hearing in fishes. Philos Trans R Soc Lond B Biol Sci 2000;355:1285–1288.
6. Zeddies DG, Fay RR. Development of the acoustically evoked behavioral response in zebrafish to pure tones. J Exp Biol 2005;208:1363–1372.
7. Cahill GM. Clock mechanisms in zebrafish. Cell Tissue Res 2002;30:27–34.
8. Hirayama J, Kaneko M, Cardone L, Cahill G, Sassone-Corsi P. Analysis of circadian rhythms in zebrafish. Methods Enzymol 2005;393:186–204.
9. Lahiri K, Vallone D, Gondi SB, Santoriello C, Dickmeis T, Foulkes NS. Temperature regulates transcription in the zebrafish circadian clock. PLoS Biol 2005;3:e351.

10. Fox HE, White SA, Kao MH, and Fernald RD. Stress and dominance in a social fish. J Neurosci 1997;17:6463–6469.
11. Larson ET, O'Malley DM, Melloni RH Jr. Aggression and vasotocin are associated with dominant-subordinate relationships in zebrafish. Behav Brain Res 2006;167:94–102.
12. Overli O, Korzan WJ, Hoglund E, Winberg S, Bollig H, Watt M, et al. Stress coping style predicts aggression and social dominance in rainbow trout. Horm Behav 2004;45:235–241.
13. Overli O, Korzan WJ, Larson ET, Winberg S, Lepage O, Pottinger TG, et al. Behavioral and neuroendocrine correlates of displaced aggression in trout. Horm Behav 22004;45:324–329.
14. Baraban SC, Taylor MR, Castro PA, Baier H. Pentylenetetrazole induced changes in zebrafish behavior, neural activity and c-fos expression. Neuroscience 2005;131:759–768.
15. Bretaud S, Lee S, Guo S. Sensitivity of zebrafish to environmental toxins implicated in Parkinson's disease. Neurotoxicol Teratol 2004;26:857–864.
16. Gerlai R, Lahav M, Guo S, Rosenthal A. Drinks like a fish: zebra fish (*Danio rerio*) as a behavior genetic model to study alcohol effects. Pharmacol Biochem Behav 2000;67:773–782.
17. Lam CS, Korzh V, Strahle U. Zebrafish embryos are susceptible to the dopaminergic neurotoxin MPTP. Eur J Neurosci 2005;21:1758–1762.
18. Levin E, Chen E. Nicotinic involvement in memory function in zebrafish. Neurotoxicol Teratol 2004;26: 731–735.
19. Lockwood B, Bjerke S, Kobayashi K, Guo S. Acute effects of alcohol on larval zebrafish: a genetic system for large-scale screening. Pharma Biochem Behav 2004;77:647–654.
20. Scalzo FM, Levin ED. (2004). The use of zebrafish (*Danio rerio*) as a model system in neurobehavioral toxicology. Neurotoxicol Teratol 2004;26:707–708.
21. Brustein E, Marandi N, Kovalchuk Y, Drapeau P, Konnerth A. "In vivo" monitoring of neuronal network activity in zebrafish by two-photon Ca(2+) imaging. Pflugers Arch 2003;446:766–773.
22. Higashijima S, Masino MA, Mandel G, Fetcho JR. Imaging neuronal activity during zebrafish behavior with a genetically encoded calcium indicator. J Neurophysiol 2003;90:3986–3997.
23. Masino MA, Fetcho JR. Fictive swimming motor patterns in wild type and mutant larval zebrafish. J Neurophysiol 2005;93:3177–3188.

ABOUT THE AUTHORS

Ádám Miklósi and Richard Andrew

Professor Richard Andrew and Ádám Miklósi have been working on behavioral lateralization in the zebrafish. Initially, their primary interest was to describe such behavioral traits in the zebrafish in order to reveal possible homologies between mammals and fishes. They think that the zebrafish provides a very good model for the understanding of behavioral lateralization due to its well-known genetic and developmental organization. Richard Andrew is now interested in the lateralized control of memory processes in the zebrafish larvae.

Stephan Neuhauss

Work in the laboratory of Stephan Neuhauss addresses the function of the developing zebrafish visual system. It was instrumental in establishing behavioral and physiological paradigms to screen for mutant strains with vision deficits. This genetic approach has yielded a number of visually impaired mutant strains that will be central to an analysis of the molecular working of the vertebrate retina and associated human ocular diseases.

Pertti Panula

The laboratory of Pertti Panula focuses on the role of modulatory neurotransmitters (e.g., amines and neuropeptides) on complex behaviors and brain diseases. Especially imaging systems of complex networks, and automated behavioral analysis methods have been developed in the laboratory. They are applied in functional analysis of zebrafish orthologs of human disease genes using a multidisciplinary approach.

Cosme Salas

The Laboratory of Psychobiology of the University of Sevilla focuses on behavioral neuroscience from a comparative point of view. A major topic is the study of the neural basis of learning and memory in teleost fish using a combination of behavioral, neurophysiological, and neuroanatomical approaches.

Louis Saint-Amant

Louis Saint-Amant was a Ph.D. student in the laboratory of Dr. Pierre Drapeau where he worked on the development of embryonic spinal circuits in zebrafish. He is currently a postdoctoral fellow in the laboratory of Dr. John Kuwada. The Kuwada laboratory is interested the genetics of neural development and is currently using a mutagenesis approach in zebrafish to find genes required for CNS development and function.

Helene Volkoff and Richard E. Peter

Helene Volkoff and Richard Peter have jointly undertaken extensive research on the endocrine regulation of feeding in teleost fish. Research has involved use of a wide range of techniques, including stereotaxic brain injections of synthetic peptides, and molecular techniques such as cDNA cloning and gene expression studies. A model for the regulation of food intake in fish has been developed. Research in H. Volkoff's laboratory now focuses on the endocrine mechanisms regulating food intake and feeding behavior in fish using goldfish and marine teleosts as models. R.E. Peter's research pertains to the neuroendocrine regulation of secretion of gonadotropins and growth hormone in teleost fish, as well as the regulation of food intake and feeding behavior. Models for the neuroendocrine regulation of reproduction and growth hormone release in fish have been developed.

Kathleen Whitlock

Work in the laboratory of Kathleen Whitlock addresses the development of the olfactory sensory system and the associated neuroendocrine cells containing gonadotropin-releasing hormone (GnRH). The laboratory has pioneered use of olfactory response in zebrafish for a genetic screen, and more recently has used gene expression as a read-out for epigenetic changes resulting from olfactory imprinting. This work was instrumental in demonstrating that zebrafish make and maintain olfactory memories which result in correlated epigenetic changes in the olfactory sensory epithelia. In tandem, the lab has shown that the essential GnRH containing cells of the hypothalamus do not arise from the olfactory placode, rather they arise from multiple embryonic origins outside the olfactory placode. The intimate association of olfaction and reproduction suggests a physiological and perhaps a developmental modulation of the olfactory epithelia by GnRH.

Dominic Wright and Jens Krause

The general aim of the Fish Behaviour Group at Leeds (Krause laboratory) is to investigate the social organization of fish with a focus on the mechanisms and functions of shoaling behavior. To achieve this aim, one approach is to conduct studies on behavioral genetics and integrate them with information on social networks. Dominic Wright completed his Ph.D. on the genetics of behavior in the zebrafish at Leeds University and is now investigating the genetics of behavior in the chicken at Linköping University.

Irina Zhdanova

Work in the laboratory of Dr. Zhdanova addresses the role of the neurohumoral factors in sleep and circadian rhythms regulation. It was instrumental in characterizing sleep in zebrafish and finding that the pineal hormone melatonin is a sleep-promoting factor in diurnal vertebrates, including nonhuman primates and zebrafish.

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1. Caroline H. Brennan. 2011. Zebrafish behavioural assays of translational relevance for the study of psychiatric disease. *Reviews in the Neurosciences* **22**:1. . [CrossRef]