Social Regulation of Neurogenesis in Teleosts

Christina Sørensen[a]   Øyvind Øverli[b, c]   Cliff H. Summers[c, d]   Göran E. Nilsson[a]

[a] Department of Molecular Biosciences, University of Oslo, Oslo, [b] Department of Animal and Aquacultural Sciences, Norwegian University of Life Sciences, Ås, Norway; [c] Department of Biology, University of South Dakota, [d] Neuroscience Group, Division of Basic Biomedical Science, Sanford School of Medicine, University of South Dakota, Vermillion, S. Dak., USA

Abstract
Salmonid fishes such as the rainbow trout *(Oncorhynchus mykiss)* are frequently used to study behavioral and neuroendocrine effects of socially induced stress. A predictable aggressive response to territorial intrusion, a well described neuroanatomy, and many essential similarities in the stress response in fishes and other vertebrates are among the advantages of this comparative model. One conspicuous difference when compared to mammals, however, is that in telost fish and other non-mammalian vertebrates, neurogenesis persists into adulthood to a much higher degree. Very little is known about the functional significance of individual differences in the rate of brain cell proliferation in fish, or whether structural changes in the fish brain are influenced by the social environment. In this paper we discuss the observation that brain cell proliferation is reduced in subordinate fish, focusing in particular on whether such individual variation reflects a difference in coping style or is indeed a response to social interactions.

Copyright © 2007 S. Karger AG, Basel

Introduction: Rainbow Trout as a Model of Social Stress

In teleost fish, as in other vertebrates, individuals that have recently lost fights or hold a subordinate position in a stable social hierarchy often show a general behavioral inhibition, characterized by suppressed aggressive and reproductive behavior, reduced feeding, and low locomotor activity [Abbott et al., 1985; Francis et al., 1993; Huntingford et al., 1993; Winberg and Nilsson, 1993; Winberg et al., 1993; Oliveira and Almada, 1998; Øverli et al., 1998; Höglund et al., 2001; Gomez-Laplaza and Morgan, 2003; Amorim and Almada, 2005; Black et al., 2005; Hsu et al., 2006]. Physiologically, subordinate fish show many of the signs of prolonged stress that are commonly observed in mammals, including elevated hypothalamus-pituitary-interrenal (HPI) axis activity, decreased hypothalamus-pituitary-gonadal (HPG) activity, and chronically increased brain serotonin (5-hydroxytryptamin, 5-HT) metabolism [Winberg et al., 1992; Winberg and Nilsson, 1993; Francis et al., 1993; Fox et al., 1997; Winberg and Lepage, 1998; Øverli et al., 1999; Elofsson et al., 2000; Höglund et al., 2000; Bass and Grober, 2001; Doyon et al., 2003; Parikh et al., 2006].

Social modulation of behavior is particularly distinct in small groups of salmonid fish, in which the fish can be highly aggressive and territorial both in nature and under

Christina Sørensen
Department of Molecular Biosciences, University of Oslo
PO Box 1041 Blindern, NO–0316 Oslo (Norway)
Tel. +47 2285 5785, Fax +47 2285 6041
E-Mail christina.sorensen@imbv.uio.no

conditions of rearing in captivity. Migratory salmonids are pre-eminently territorial at life stages when they reside in rivers, and clear dominance/subordination relationships form in experimentally established pairs of juvenile salmonids. In such assemblages, dominant individuals can often be seen to monopolize food, and initiate virtually all aggressive acts [Øverli et al., 1998, 1999; Höglund et al., 2002].

Rainbow trout *(Oncorhynchus mykiss)* is one of the most commonly used fish species in biological studies [Thorgaard et al., 2002]. It is also one of the most aggressive salmonid species, and has been used in a range of influential studies on the neuroendocrine and behavioral correlates of social position [see, e.g., original papers by Pottinger and Pickering, 1992; Johnsson and Björnsson, 1994; Winberg and Lepage, 1998; Øverli et al., 1999; Sloman et al., 2001, and reviews by Sloman and Armstrong, 2002; Gilmour et al., 2005; Summers and Winberg, 2006]. The neuroanatomy of salmonid fish has also been extensively studied [Northcutt and Bradford, 1980; Billard and Peter, 1982; Holmqvist and Ekström, 1995; Teitsma et al., 1999; Carruth et al., 2000; Vetillard et al., 2002]. This crucial knowledge, in combination with a predictable aggressive response to territorial intrusion, makes salmonid species such as the rainbow trout ideal for comparative studies of the neuroendocrine correlates of social position. A particularly advantageous aspect of the behavior of domesticated rainbow trout is that these fish easily adapt to new environments, including rearing in isolation. A period of isolation prior to the construction of new social groups is often an essential part of experimental design, serving to minimize the effect of previous social interactions, or to reveal trait characters that predict social position [Øverli et al., 2004].

The Interaction between Social Position and Stress Coping Style

A caveat of all research on social interactions is the inherent difficulty in determining which traits are causes and which are consequences of social position. Behavioral inhibition in subordinate animals can be viewed as a passive coping response serving to avoid costly interactions with aggressive dominant individuals [Leshner, 1980]. It has, however, also been firmly established that coping style has a genetic component [Driscoll et al., 1998; Koolhaas et al., 1999; Lepage et al., 2000; Ellenbroek and Cools, 2002; de Boer et al., 2003; Veenema et al., 2003]. In rainbow trout, the magnitude of the cortisol response to stress shows both

consistency over time and a moderate to high degree of heritability, and high-responding (HR) and low-responding (LR) lines of rainbow trout have been generated by individual selection for consistently high or low post-stress cortisol values [Pottinger and Carrick, 1999]. Genetically determined differences in HPI-axis activity affect social standing in such a way that LR fish usually win fights for social dominance [Pottinger and Carrick, 2001]. Other studies suggested that LR fish are also characterized by a rapid recovery of food intake after transfer to a novel environment, and a reduced locomotor response in a territorial intrusion test [Øverli et al., 2001, 2002]. Hence, some of the features of the LR trout line suggest that they represent selection for a proactive stress coping style, as defined by Koolhaas et al. [1999]. It should, however, also be pointed out that the behavior of the HR-LR lines of fish is highly context dependent, and are influenced by factors such as novelty of the environment and group size [Schjolden et al., 2005, 2006; Schjolden and Winberg, 2007]. The apparent parallel to genetically determined stress coping styles in mammals, and the existence of similar trait associations in unselected populations of rainbow trout [Øverli et al., 2004, 2006] nevertheless suggest an evolutionarily conserved correlation among multiple traits.

Based on the observation that rapid resumption of food intake in a new environment is a highly predictable indicator of the outcome of fights for dominance in both fish and *Anolis* lizards [Øverli et al., 2004; Korzan et al., 2006], Summers et al. [2005] were able to demonstrate a range of region-specific differences in brain serotonergic function between presumptive dominant and subordinate animals while they were still kept in isolation. Hence, there is every reason to think that some of the physiological and behavioral characteristics that have previously been interpreted as effects of rank might in reality reflect pre-existing individual variation. On the other hand, it has been shown that individuals retain the capacity to rapidly change their physiology and behavior in response to social opportunity [Burmeister et al., 2005; Burmeister, 2007]. In any case, subordination and chronic stress might alter hormone feedback and responsiveness, and perhaps reinforce pre-existing differences, so that dominant and subordinate individuals will respond differently to any intended and unintended experimental stressor. Contradictions in the literature on social interactions and stress have been pointed out by several reviewers [e.g., Creel, 2001; Honess and Marin, 2006], and interactions between inherited differences in stress coping style and acute and chronic effects of social position are likely to be responsible for many of these.

Adult neurogenesis and other forms of structural plasticity in the brain have received much attention in association with social stress. Reduced hippocampal neurogenesis appears to be central to the pathophysiology of chronic stress and depression [Dranovsky and Hen, 2006; Warner-Schmidt and Duman, 2006]. Adult hippocampal neurogenesis also represents an intercept between the 5-HT system and the HPA axis. Thus measuring neurogenesis in animal models of social stress and stress coping styles might shed new light on the dynamics of these systems. In line with the topic of this symposium, the rest of this paper is devoted to discussing differences in neurogenesis between dominant and subordinate animals, focusing in particular on whether such individual variation reflects a difference in coping style or is indeed a response to social interactions.

Linking Physiological, Behavioral and Cognitive Traits – Possible Role of Neurogenesis

A long standing dogma in neuroscience was that the adult mammalian brain is incapable of cell renewal. It is, however, currently agreed that new neurons and glial cells are generated in the brain of adult individuals from all major vertebrate taxa, a process known as adult neurogenesis [Eriksson et al., 1998; Gould et al., 1999a; Biebl et al., 2000; Gross, 2000; Garcia-Verdugo et al., 2002; Nottebohm, 2002; Kempermann et al., 2004; Laplagne et al., 2006; Ramirez-Amaya et al., 2006]. Adult neurogenesis in the hippocampus has received much attention, as it appears to be highly important for behavior, mood and cognition in both animals and humans, and is affected by a range of environmental, endocrine, and pharmacological factors [Bodnoff et al., 1995, Gould et al., 1997, 1998, 1999b; Brezun and Daszuta, 1999; Duman et al., 2001; Nilsson et al., 1999; Jacobs et al., 2000; Shors et al., 2001; Lipkind et al., 2002; Malberg and Duman, 2003; Sapolsky, 2003; Huang and Herbert, 2005; Vaynman and Gomez-Pinilla, 2006; Fuchs et al., 2006].

In particular, stress and glucocorticoid exposure have been shown to reduce adult hippocampal cell proliferation [Gould et al., 1992; Cameron and Gould, 1994; Cameron et al., 1995; McEwen, 1996], whereas voluntary exercise [van Praag et al., 1999a, b] and environmental enrichment do the opposite [Kempermann et al., 1997; Nilsson et al., 1999]. Not surprisingly, then, the experience of social subordination leads to reduced neurogenesis [Gould et al., 1997, 1998; Blanchard et al., 2001].

In animal models of depression, and not only those utilizing social stress, a general behavioral inhibition is often seen after chronic, severe, or unpredictable stressors [Willner, 1990; Weiss and Kilts, 1998; Anisman and Matheson, 2005]. Treatment with anti-depressants such as serotonin reuptake inhibitors increases neurogenesis [Malberg et al., 2000; Duman et al., 2001], and prevents both the reduction in neurogenesis and the behavioral inhibition associated with stress [Czéh et al., 2001; Malberg and Duman, 2003]. Schmidt-Hieber et al. [2004] showed that associative long-term potentiation can be induced more easily in young neurons than in mature neurons under identical conditions. These authors raised the hypothesis that newly generated neurons express unique mechanisms to facilitate synaptic plasticity, which might be important for the formation of new memories. Consequently, newborn hippocampal neurons are assumed to have a central function in cognition [Aimone et al., 2006]. Reduced cognitive performance, i.e., reduced ability to interpret a situation based on previous experience, might reduce predictability and control, and hence promote passive, or reactive, behavioral stress responses.

The question of whether genetically determined differences in stress coping style also incur differences in hippocampal cell proliferation was addressed by Veenema et al. [2004]. Working with the long (LAL) and short (SAL) attack latency mouse strains, these authors found that hippocampal cell proliferation was less affected by stress in the proactive and aggressive SAL mice. Higher glucocorticoid levels and reduced 5-HT signaling [Veenema et al., 2003, 2004; Veenema and Neumann, 2007] in the LAL mice might be contributing to this difference. Genetic influence on hippocampal neurogenesis has also been shown in several other studies [Hayes and Nowakowski, 2002; Kempermann and Gage, 2002; Schauwecker, 2006; Kronenberg et al., 2007]. The observation that social stress affects neurogenesis [Gould et al., 1997] and structural plasticity in the brain [Magarinos et al., 1996; Fuchs and Flügge, 2003] has received wide attention, but the possible interaction between these effects and pre-existing differences in stress coping style is less studied.

Effect of Social Stress on Telencephalic Cell Proliferation in Rainbow Trout

Compared to mammals, neurogenesis persists into adulthood to a much higher degree in the central nervous system of teleost fish and other ectothermic vertebrates
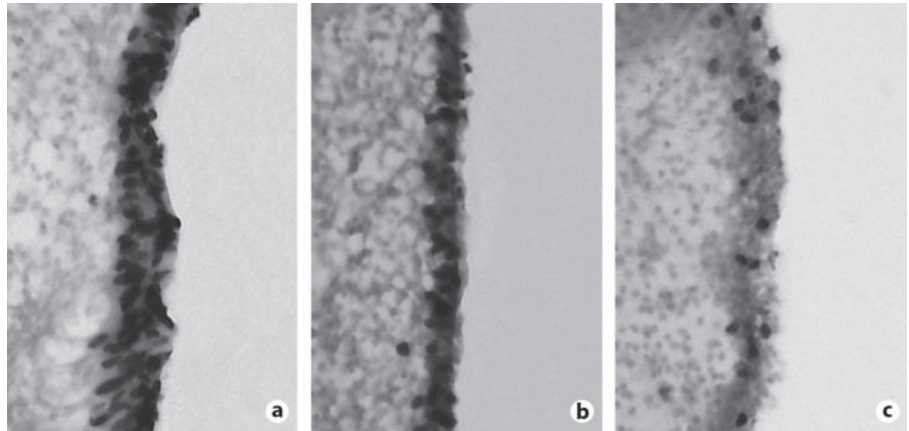
Fig. 1. BrdU-positive cells in the dorsal and ventral nuclei of the ventral telencephalon of (**a**) control, (**b**) dominant and (**c**) subordinate fish.

[Font et al., 2001; Zupanc, 2001a, 2006]. The number of brain cells increases with age, body weight, and body length in teleosts [Birse et al., 1980; Zupanc and Horschke, 1995], and specific regions of active cell division, proliferation zones, have been found in all major brain areas of adult fish [Zupanc and Horsche, 1995; Ekström et al., 2001; Zupanc et al., 2005]. The continuous generation of cells contributes to the well-documented ability of fish to regenerate parts of the central nervous system after injury [Stuermer et al., 1992; Zupanc and Ott, 1999]. As commented by Zupanc [2001b], this impressive degree of proliferation makes it particularly interesting to examine adult neurogenesis from a comparative point of view. Very little is, however, known about the regulation and functional significance of neurogenesis in teleost fish.

In a recent experiment [Sørensen, 2005], pairs of rainbow trout were allowed to fight for dominance, and were then left to interact for 4 days. The thymidine analogue 5-bromodeoxyuridine (BrdU) was administered intraperitoneally to all fish 24 h prior to the end of the experiment. Through incorporation into the DNA of cells going through S-phase, BrdU acts as a marker of proliferation. Proliferating cells were visualized immunohistochemically and quantified in transverse sections of the telencephalon, in which areas homologous to the mammalian hippocampus are thought to be located based on both anatomical and functional evidence [Northcutt and Bradford, 1980; Butler, 2000; Rodríguez et al., 2002; Portavella et al., 2004].

Brain stem monoamine metabolism and plasma cortisol were analysed in fish from the same experiment. These data confirmed that subordinate fish were chronically stressed, for instance showing significantly elevated concentrations of the serotonin metabolite 5-hydroxyin-

dole acetic acid (5-HIAA concentrations in control, dominant, and subordinate fish, respectively, were: 69.7 ± 10.1 ng/g, 73.7 ± 10.2 ng/g, and 105.8 ± 10.8 ng/g, with $F_{(2,26)} = 3.5$, $p = 0.04$) and increased plasma cortisol concentrations (cortisol in control, dominant, and subordinate fish, respectively, were: 33.3 ± 9.2 ng/ml, 22.9 ± 6.7 ng/ml, and 88.0 ± 22.4 ng/ml in control, dominant, and subordinate fish, respectively, with $F_{(2,29)} = 6.0$, $p = 0.007$). As expected, subordinate individuals also showed reduced forebrain cell proliferation (stained nuclei/mm^3 in control, dominant, and subordinate fish, respectively, were: 2,041 ± 224, 1,634 ± 141, and 1,276 ± 76, with $F_{(2,12)} = 5.8$, $p = 0.02$) (fig. 1). The data suggests that social interaction leads to reduced cell proliferation in both dominant and subordinate fish, although more so in subordinate fish, which was the only group where appropriate post-hoc comparisons revealed a statistically significant difference compared to controls. If the lower proliferation seen in subordinate fish only reflects a pre-existing difference, one would expect the control group (a random selection of isolated, non-disturbed animals) to contain an equal number of presumptive dominant and presumptive subordinate individuals. This group should then be intermediate to both other groups. Instead, the intermediate values are displayed by the dominant fish.

Further evidence from behavioral analysis also suggests that aggressive social interactions have a major influence on brain cell proliferation. Daily observation of the frequency of aggressive acts in each pair revealed that the aggression received by subordinate fish on the first day of interaction correlated negatively with the number of BrdU marked cells in the telencephalon (Pearson $r^2 = 0.77$, $p = 0.05$). Neither the number of aggressive acts received on the final day of interaction ($R^2 = 0.14$, $p = 0.53$),

nor the total number of aggressive acts received during the whole observation period ($R^2 = 0.13$, $p = 0.55$) showed any trend towards such a relationship. The number of subordinate fish that was subject to the BrdU immunohistochemistry (n = 5) is too low to allow firm conclusions based on correlative measures. The observation that initial aggression is important, but not what happens afterwards, also seems somewhat contradictory. It should, however, be pointed out that a previous study also showed that it was, in fact, aggression received at the earliest stages of hierarchy formation that determined neuroendocrine impact in subordinates [Winberg and Lepage, 1998].

In comparison, a recent study by Mitra et al. [2006] found that individual differences in hippocampal cell proliferation in intruder rats was not related to aggression received by the subject, but rather to the frequency of defensive behavior shown by each test subject. These authors concluded that individual differences in stress-related behavior influenced cell proliferation in the mouse hippocampus.

It is, however, not unlikely that there also could have been a pre-existing difference between the individuals assuming dominant and subordinate positions. The groups' differing levels of cell proliferation could reflect a pre-existing difference in the vulnerability to social stress. This is obviously complicated by the fact that the subordinate fish are exposed to a completely different stress level than dominant fish while in the hierarchy, accompanied by differences both in cortisol levels and 5-HT activity.

It is becoming increasingly more evident that genetic factors are highly important in determining predisposition for depressive disorders [Hayes and Nowakowski, 2002; Kempermann and Gage, 2002; Schauwecker, 2006; Kronenberg et al., 2007] Also, the fact that the previously mentioned SAL and LAL mouse strains display differences in baseline neurogenesis [Veenema et al., 2004], not only indicates that there could be a distribution of baseline neurogenic rates in a natural population, but also that these could, indeed, correspond with stress coping style. One can only speculate on whether a reduced baseline neurogenesis in itself would be a determining factor for social subordination, or if it appears as a side effect of other factors that predispose an individual for a subordinate position. As previously mentioned, behavior in isolation can predict social position in rainbow trout [Øverli et al., 2004] in the same way as in *Anolis* lizards [Korzan et al., 2006]. Thus it would be of huge interest to expose animals predicted to be dominant and subordinate in an otherwise equal pair to either social dominance or subordination through pairing with smaller or larger animals. Together with an investigation of baseline neurogenesis performed on a larger selection of animals this could shed light on whether the rate of neurogenesis is a determining factor for social position, a side effect of other inherent traits or merely a product of a stressful situation.

References

Abbott JC, Dunbrack RL, Orr CD (1985) The interaction of size and experience in dominance relationships of juvenile steelhead trout *(Salmo gairdneri).* Behaviour 92:241–253.

Aimone JB, Wiles J, Gage FH (2006) Potential role for adult neurogenesis in the encoding of time in new memories. Nature Neurosci 9:723–727.

Amorim MCP, Almada VC (2005) The outcome of male-male encounters affects subsequent sound production during courtship in the cichlid fish *Oreochromis mossambicus.* Anim Behav 69:595–601.

Anisman H, Matheson K (2005) Stress, depression, and anhedonia: Caveats concerning animal models. Neurosci Biobehav Rev 29:525–546.

Bass AH, Grober MS (2001) Social and neural modulation of sexual plasticity in teleost fish. Brain Behav Evol 57:293–300.

Biebl M, Cooper CM, Winkler J, Kuhn HG (2000) Analysis of neurogenesis and programmed cell death reveals a self-renewing capacity in the adult rat brain. Neurosci Lett 291:17–20.

Billard R, Peter RE (1982) A stereotaxic atlas and technique for nuclei of the diencephalon of rainbow trout *(Salmo gairdneri).* Reprod Nutr Dev 22:1–25.

Birse SC, Leonard RB, Coggeshall RE (1980) Neuronal increase in various areas of the nervous system of the guppy, *Lebistes.* J Comp Neurol 194:291–301.

Black MP, Balthazart J, Baillien M, Grober MS (2005) Socially induced and rapid increases in aggression are inversely related to brain aromatase activity in a sex-changing fish, *Lythrypnus dalli.* Proc R Soc B 272:2435–2440.

Blanchard RJ, McKittrick CR, Blanchard DC (2001) Animal models of social stress: Effects on behavior and brain neurochemical systems. Physiol Behav 73:261–271.

Bodnoff SR, Humphreys AG, Lehman JC, Diamond DM, Rose GM, Meaney MJ (1995) Enduring effects of chronic corticosterone treatment on spatial-learning, synaptic plasticity, and hippocampal neuropathology in young and mid-aged rats. J Neurosci 15:61–69.

Brezun JM, Daszuta A (1999) Depletion in serotonin decreases neurogenesis in the dentate gyrus and the subventricular zone of adult rats. Neuroscience 89:999–1002.

Burmeister SS (2007) Genomic responses to behavioral interactions in an African cichlid fish: mechanisms and evolutionary implications. Brain Behav Evol 70:247–256.

Burmeister SS, Jarvis ED, Fernald RD (2005) Rapid behavioral and genomic responses to social opportunity. Plos Biol 3:1996–2004.

Butler AB (2000) Topography and topology of the teleost telencephalon: a paradox resolved. Neurosci Lett 293:95–98.

Cameron HA, Gould E (1994) Adult neurogenesis is regulated by adrenal steroids in the dentate gyrus. Neuroscience 61:203–209.

Cameron HA, McEwen BS, Gould E (1995) Regulation of adult neurogenesis by excitatory input and NMDA receptor activation in the dentate gyrus. J Neurosci 15:4687–4692.

Carruth LL, Jones RE, Norris DO (2000) Cell density and intracellular translocation of glucocorticoid receptor-immunoreactive neurons in the kokanee salmon (Oncorhynchus nerka kennerlyi) brain, with an emphasis on the olfactory system. Gen Comp Endocrinol 117:66–76.

Creel S (2001) Social dominance and stress hormones. Trends Ecol Evol 16:491–497.

de Boer SF, van der Vegt BJ, Koolhaas JM (2003) Individual variation in aggression of feral rodent strains: A standard for the genetics of aggression and violence? Behav Genet 33:485–501.

Czéh B, Michaelis T, Watanabe T, Frahm J, de Biurrun G, van Kampen M, Bartolomucci A, Fuchs E (2001) Stress-induced changes in cerebral metabolites, hippocampal volume, and cell proliferation are prevented by antidepressant treatment with tianeptine. Proc Natl Acad Sci USA 98:12796–12801.

Doyon C, Gilmour KM, Trudeau VL, Moon TW (2003) Corticotropin-releasing factor and neuropeptide Y mRNA levels are elevated in the preoptic area of socially subordinate rainbow trout. Gen Comp Endocrinol 133:260–271.

Dranovsky A, Hen R (2006) Hippocampal neurogenesis: Regulation by stress and antidepressants. Biol Psych 59:1136–1143.

Driscoll P, Escorihuela RM, Fernandez-Teruel A, Giorgi O, Schwegler H, Steimer T, Wiersma A, Corda MG, Flint J, Koolhaas JM, Langhans W, Schulz PE, Siegel J, Tobena A (1998) Genetic selection and differential stress responses – The Roman lines/strains of rats. In: Stress of Life (Csermely P, ed.) vol 851, pp 501–510. New York: New York Academy of Sciences.

Duman RS, Nakagawa S, Malberg J (2001) Regulation of adult neurogenesis by antidepressant treatment. Neuropsychopharmacology 25:836–844.

Ekström P, Johnsson CM, Ohlin LM (2001) Ventricular proliferation zones in the brain of an adult teleost fish and their relation to neuromeres and migration (secondary matrix) zones. J Comp Neurol 436:92–110.

Ellenbroek BA, Cools AR (2002) Apomorphine susceptibility and animal models for psychopathology: Genes and environment. Behav Genet 32:349–361.

Elofsson UOE, Mayer I, Damsgård B, Winberg S (2000) Intermale competition in sexually mature arctic charr: Effects on brain monoamines, endocrine stress responses, sex hormone levels, and behavior. Gen Comp Endocrinol 118:450–460.

Eriksson PS, Perfilieva E, Björk-Eriksson T, Alborn AM, Nordborg C, Peterson DA, Gage FH (1998) Neurogenesis in the adult human hippocampus. Nat Med 4:1313–1317.

Font E, Desfilis E, Perez-Canellas MM, Garcia-Verdugo JM (2001) Neurogenesis and neuronal regeneration in the adult reptilian brain. Brain Behav Evol 58:276–295.

Fox HE, White SA, Kao MHF, Fernald RD (1997) Stress and dominance in a social fish. J Neurosci 17:6463–6469.

Francis RC, Soma K, Fernald RD (1993) Social regulation of the brain pituitary gonadal axis. Proc Natl Acad Sci USA 90:7794–7798.

Fuchs E, Flügge G (2003) Chronic social stress: effects on limbic brain structures. Physiol Behav 79:417–427.

Fuchs E, Flügge G, Czeh B (2006) Remodeling of neuronal networks by stress. Front Biosci 11:2746–2758.

Garcia-Verdugo JM, Ferron S, Flames N, Collado L, Desfilis E, Font E (2002) The proliferative ventricular zone in adult vertebrates: A comparative study using reptiles, birds, and mammals. Brain Res Bull 57:765–775.

Gilmour KM, DiBattista JD, Thomas JB (2005) Physiological causes and consequences of social status in salmonid fish. Integr Comp Biol 45:263–273.

Gomez-Laplaza LM, Morgan E (2003) The influence of social rank in the angelfish, Pterophyllum scalare, on locomotor and feeding activities in a novel environment. Lab Anim 37:108–120.

Gould E, Cameron HA, Daniels DC, Woolley CS, McEwen BS (1992) Adrenal hormones suppress cell division in the adult-rat dentate gyrus. J Neurosci 12:3642–3650.

Gould E, McEwen BS, Tanapat P, Galea LAM, Fuchs E (1997) Neurogenesis in the dentate gyrus of the adult tree shrew is regulated by psychosocial stress and NMDA receptor activation. J Neurosci 17:2492–2498.

Gould E, Tanapat P, McEwen BS, Flügge G, Fuchs E (1998) Proliferation of granule cell precursors in the dentate gyrus of adult monkeys is diminished by stress. Proc Natl Acad Sci USA 95:3168–3171.

Gould E, Reeves AJ, Graziano MSA, Gross CG (1999a) Neurogenesis in the neocortex of adult primates. Science 286:548–552.

Gould E, Beylin A, Tanapat P, Reeves A, Shors TJ (1999b) Learning enhances adult neurogenesis in the hippocampal formation. Nat Neurosci 2:260–265.

Gross CG (2000) Neurogenesis in the adult brain: death of a dogma. Nat Rev Neurosci 1:67–73.

Hayes NL, Nowakowski RS (2002) Dynamics of cell proliferation in the adult dentate gyrus of two inbred strains of mice. Dev Brain Res 134:77–85.

Höglund E, Balm PHM, Winberg S (2000) Skin darkening, a potential social signal in subordinate Arctic charr (Salvelinus alpinus): The regulatory role of brain monoamines and pro-opiomelanocortin-derived peptides. J Exp Biol 203:1711–1721.

Höglund E, Kolm N, Winberg S (2001) Stress-induced changes in brain serotonergic activity, plasma cortisol and aggressive behavior in Arctic charr (Salvelinus alpinus) is counteracted by L-DOPA. Physiol Behav 74:381–389.

Höglund E, Balm PHM, Winberg S (2002) Behavioural and neuroendocrine effects of environmental background colour and social interaction in Arctic charr (Salvelinus alpinus). J Exp Biol 205:2535–2543.

Holmqvist BI, Ekström P (1995) Hypophysiotrophic systems in the brain of the Atlantic salmon. Neuronal innervation of the pituitary and the origin of pituitary dopamine and nonapeptides identified by means of combined carbocyanine tract tracing and immunocytochemistry. J Chem Neuroanat 8:125–145.

Honess PE, Marin CM (2006) Behavioural and physiological aspects of stress and aggression in nonhuman primates. Neurosci Biobehav Rev 30:390–412.

Hsu YY, Earley RL, Wolf LL (2006) Modulation of aggressive behaviour by fighting experience: mechanisms and contest outcomes. Biol Rev 81:33–74.

Huang GJ, Herbert J (2005) The role of 5-HT$_{1A}$ receptors in the proliferation and survival of progenitor cells in the dentate gyrus of the adult hippocampus and their regulation by corticoids. Neuroscience 135:803–813.

Huntingford FA, Metcalfe NB, Thorpe JE (1993) Social status and feeding in Atlantic salmon Salmo salar Parr: the effect of visual exposure to a dominant. Ethology 94:201–206.

Jacobs BL, van Praag H, Gage FH (2000) Adult brain neurogenesis and psychiatry: a novel theory of depression. Mol Psychiatry 5:262–269.

Johnsson JI, Björnsson BT (1994) Growth hormone increases growth rate, appetite and dominance in juvenile rainbow trout, Oncorhynchus mykiss. Anim Behav 48:177–186.

Kempermann G, Kuhn HG, Gage FH (1997) More hippocampal neurons in adult mice living in an enriched environment. Nature 386:493–495.

Kempermann G, Gage FH (2002) Genetic influence on phenotypic differentiation in adult hippocampal neurogenesis. Dev Brain Res 134:1–12.

Kempermann G, Wiskott L, Gage FH (2004) Functional significance of adult neurogenesis. Curr Opin Neurobiol 14:186–191.

Koolhaas JM, Korte SM, De Boer SF, Van Der Vegt BJ, Van Reenen CG, Hopster H, De Jong IC, Ruis MAW, Blokhuis HJ (1999) Coping styles in animals: current status in behavior and stress-physiology. Neurosci Biobehav Rev 23:925–935.

Korzan WJ, Øverli Ø, Summers CH (2006) Future social rank: forecasting status in the green anole *(Anolis carolinensis)*. Acta Ethol 9:48–57.

Kronenberg G, Lippoldt A, Kempermann G (2007) Two genetic rat models of arterial hypertension show different mechanisms by which adult hippocampal neurogenesis is increased. Dev Neurosci 29:124–133.

Laplagne DA, Esposito MS, Piatti VC, Morgenstern NA, Zhao CM, van Praag H, Gage FH, Schinder AF (2006) Functional convergence of neurons generated in the developing and adult hippocampus. Plos Biol 4:2349–2360.

Lepage O, Øverli Ø, Petersson E, Järvi T, Winberg S (2000) Differential stress coping in wild and domesticated sea trout. Brain Behav Evol 56:259–268.

Leshner AI (1980) The interaction of experience and neuroendocrine factors in determining behavioural adaptions to aggression. Prog. Brain. Res. 53, 427–438.

Lipkind D, Nottebohm F, Rado R, Barnea A (2002) Social change affects the survival of new neurons in the forebrain of adult songbirds. Behav Brain Res 133:31–43.

Magarinos AM, McEwen BS, Flügge G, Fuchs E (1996) Chronic psychosocial stress causes apical dendritic atrophy of hippocampal CA3 pyramidal neurons in subordinate tree shrews. J Neurosci 16:3534–3540.

Malberg JE, Eisch AJ, Nestler EJ, Duman RS (2000) Chronic antidepressant treatment increases neurogenesis in adult rat hippocampus. J Neurosci 20:9104–9110.

Malberg JE, Duman RS (2003) Cell proliferation in adult hippocampus is decreased by inescapable stress: Reversal by fluoxetine treatment. Neuropsychopharmacology 28:1562–1571.

McEwen BS (1996) Gonadal and adrenal steroids regulate neurochemical and structural plasticity of the hippocampus via cellular mechanisms involving NMDA receptors. Cell Mol Neurobiol 16:103–116.

Mitra R, Sundlass K, Parker KJ, Schatzberg AF, Lyons DM (2006) Social stress-related behavior affects hippocampal cell proliferation in mice. Physiol Behav 89:123–127.

Nilsson M, Perfilieva E, Johansson U, Orwar O, Eriksson PS (1999) Enriched environment increases neurogenesis in the adult rat dentate gyrus and improves spatial memory. J Neurobiol 39:569–578.

Northcutt RG, Bradford MR Jr (1980) New observations on the organization and evolution of the telencephalon of actinopterygian fishes. In: Comparative Neurology of the Telencephalon (Ebbesson SOE, ed.), pp 41–98. New York: Plenum Press.

Nottebohm F (2002) Neuronal replacement in adult brain. Brain Res Bull 57:737–749.

Oliveira RF, Almada VC (1998) Mating tactics and male-male courtship in the lek-breeding cichlid *Oreochromis mossambicus*. J Fish Biol 52:1115–1129.

Øverli Ø, Winberg S, Damsgård B, Jobling M (1998) Food intake and spontaneous swimming activity in Arctic char *(Salvelinus alpinus)*: role of brain serotonergic activity and social interactions. Can J Zool 76:1366–1370.

Øverli Ø, Harris CA, Winberg S (1999) Short-term effects of fights for social dominance and the establishment of dominant-subordinate relationships on brain monoamines and cortisol in rainbow trout. Brain Behav Evol 54:263–275.

Øverli Ø, Pottinger TG, Carrick TR, Øverli E, Winberg S (2001) Brain monoaminergic activity in rainbow trout selected for high and low stress responsiveness. Brain Behav Evol 57:214–224.

Øverli Ø, Pottinger TG, Carrick TR, Øverli E, Winberg S (2002) Differences in behaviour between rainbow trout selected for high- and low-stress responsiveness. J Exp Biol 205:391–395.

Øverli Ø, Korzan WJ, Höglund E, Winberg S, Bollig H, Watt M, Forster GL, Barton BA, Øverli E, Renner KJ, Summers CH (2004) Stress coping style predicts aggression and social dominance in rainbow trout. Horm Behav 45:235–241.

Øverli Ø, Sørensen C, Nilsson GE (2006) Behavioral indicators of stress-coping style in rainbow trout: Do males and females react differently to novelty? Physiol Behav 87:506–512.

Parikh VN, Clement TS, Fernald RD (2006) Androgen level and male social status in the African cichlid, *Astatotilapia burtoni*. Behav Brain Res 166:291–295.

Portavella M, Torres B, Salas C (2004) Avoidance response in goldfish: Emotional and temporal involvement of medial and lateral telencephalic pallium. J Neurosci 24:2335–2342.

Pottinger TG, Pickering AD (1992) The influence of social interaction on the acclimation of rainbow-trout, *Oncorhynchus mykiss* (Walbaum) to chronic stress. J Fish Biol 41:435–447.

Pottinger TG, Carrick TR (1999) Modification of the plasma cortisol response to stress in rainbow trout by selective breeding. Gen Comp Endocrinol 116:122–132.

Pottinger TG, Carrick TR (2001) Stress responsiveness affects dominant-subordinate relationships in rainbow trout. Horm Behav 40:419–427.

Ramirez-Amaya V, Marrone DF, Gage FH, Worley PF, Barnes CA (2006) Integration of new neurons into functional neural networks. J Neurosci 26:12237–12241.

Rodríguez F, Lopez JC, Vargas JP, Gomez Y, Broglio C, Salas C (2002) Conservation of spatial memory function in the pallial forebrain of reptiles and ray-finned fishes. J Neurosci 22:2894–2903.

Sapolsky RM (2003) Stress and plasticity in the limbic system. Neurochem Res 28:1735–1742.

Schauwecker PE (2006) Genetic influence on neurogenesis in the dentate gyrus of two strains of adult mice. Brain Res 1120:83–92.

Schjolden J, Bäckstrom T, Pulman KGT, Pottinger TG, Winberg S (2005) Divergence in behavioural responses trout *(Oncorhynchus mykiss)* with to stress in two strains of rainbow contrasting stress responsiveness. Horm Behav 48:537–544.

Schjolden J, Pulman KGT, Metcalfe NB, Winberg S (2006) Divergence in locomotor activity between two strains of rainbow trout *Oncorhynchus mykiss* with contrasting stress responsiveness. J. Fish Biol 68:920–924.

Schjolden J, Winberg S (2007) Genetically determined variation in stress responsiveness in rainbow trout: behavior and neurobiology. Brain Behav Evol 70:227–238.

Schmidt-Hieber C, Jonas P, Bischofberger J (2004) Enhanced synaptic plasticity in newly generated granule cells of the adult hippocampus. Nature 429:184–187.

Shors TJ, Miesegaes G, Beylin A, Zhao MR, Rydel T, Gould E (2001) Neurogenesis in the adult is involved in the formation of trace memories. Nature 410:372–376.

Sloman KA, Metcalfe NB, Taylor AC, Gilmour KM (2001) Plasma cortisol concentrations before and after social stress in rainbow trout and brown trout. Physiol Biochem Zool 74:383–389.

Sloman KA, Armstrong JD (2002) Physiological effects of dominance hierarchies: laboratory artifacts or natural phenomena? J Fish Biol 61:1–23.

Sørensen C (2005) Stressful social interaction reduces telencephalic cell proliferation in rainbow Trout. M.Sc. thesis, University of Oslo.

Stuermer CAO, Bastmeyer M, Bahr M, Strobel G, Paschke K (1992) Trying to understand axonal regeneration in the CNS of fish. J Neurobiol 23:537–550.

Summers CH, Korzan WJ, Lukkes JL, Watt MJ, Forster GL, Øverli Ø, Höglund E, Larson ET, Ronan PJ, Matter JM, Summers TR, Renner KJ, Greenberg N (2005) Does serotonin influence aggression? Comparing regional activity before and during social interaction. Physiol Biochem Zool 78:679–694.

Summers CH, Winberg S (2006) Interactions between the neural regulation of stress and aggression. J Exp Biol 209:4581–4589.

Teitsma CA, Anglade I, Lethimonier C, Le Drean G, Saligaut D, Ducouret B, Kah O (1999) Glucocorticoid receptor immunoreactivity in neurons and pituitary cells implicated in reproductive functions in rainbow trout: A double immunohistochemical study. Biol Reprod 60:642–650.

Thorgaard GH, Bailey GS, Williams D, Buhler DR, Kaattari SL, Ristow SS, Hansen JD, Winton JR, Bartholomew JL, Nagler JJ, Walsh PJ, Vijayan MM, Devlin RH, Hardy RW, Overturf KE, Young WP, Robison BD, Rexroad C, Palti Y (2002) Status and opportunities for genomics research with rainbow trout. Comp Biochem Physiol B 133:609–646.

van Praag H, Kempermann G, Gage FH (1999a) Running increases cell proliferation and neurogenesis in the adult mouse dentate gyrus. Nat Neurosci 2:266–270.

van Praag H, Christie BR, Sejnowski TJ, Gage FH (1999b) Running enhances neurogenesis, learning, and long-term potentiation in mice. Proc Natl Acad Sci USA 96:13427–13431.

Vaynman S, Gomez-Pinilla F (2006) Revenge of the 'sit': How lifestyle impacts neuronal and cognitive health through molecular systems that interface energy metabolism with neuronal plasticity. J Neurosci Res 84:699–715.

Veenema AH, Neumann ID (2007) Neurobiological mechanisms of aggression and stress coping: a comparative study in mouse and rat selection lines. Brain Behav Evol 70:274–285

Veenema AH, Meijer OC, de Kloet ER, Koolhaas JM (2003) Genetic selection for coping style predicts stressor susceptibility. J Neuroendocrinol 15:256–267.

Veenema AH, Koolhaas JM, De Kloet ER (2004) Basal and stress-induced differences in HPA axis, 5-HT responsiveness, and hippocampal cell proliferation in two mouse lines. Ann NY Acad Sci 1018:255–265.

Vetillard A, Benanni S, Saligaut C, Jego P, Bailhache T (2002) Localization of tyrosine hydroxylase and its messenger RNA in the brain of rainbow trout by immunocytochemistry and in situ hybridization. J Comp Neurol 449:374–389.

Warner-Schmidt JL, Duman RS (2006) Hippocampal neurogenesis: opposing effects of stress and antidepressant treatment. Hippocampus 16:239–249.

Weiss J, Kilts C (1998) Animal models of depression and schizophrenia. In: Textbook of Psychopharmacology (Schatzberg AF, Nemeroff CB, eds), pp 89–131. Washington DC: American Psychiatric Press.

Willner P (1990) Animal models of depression – an overview. Pharmacol Ther 45:425–455.

Winberg S, Nilsson GE, Olsén KH (1992) Changes in brain serotonergic activity during hierarchical behavior in arctic charr (*Salvelinus alpinus* L) are socially induced. J Comp Physiol A 170:93–99.

Winberg S, Nilsson GE (1993) Roles of brain monoamine neurotransmitters in agonistic behavior and stress reactions, with particular reference to fish. Comp Biochem Physiol 106:597–614.

Winberg S, Nilsson GE, Spruijt BM, Höglund U (1993) Spontaneous locomotor-activity in arctic charr measured by a computerized imaging technique – role of brain serotonergic activity. J Exp Biol 179:213–232.

Winberg S, Lepage O (1998) Elevation of brain 5-HT activity, POMC expression, and plasma cortisol in socially subordinate rainbow trout. Am J Physiol R 43:645–654.

Zupanc GKH, Horschke I (1995) Proliferation zones in the brain of adult gymnotiform fish – a quantitative mapping study. J Comp Neurol 353:213–233.

Zupanc GKH, Ott R (1999) Cell proliferation after lesions in the cerebellum of adult teleost fish: Time course, origin, and type of new cells produced. Exp Neurol 160:78–87.

Zupanc GKH (2001a) Adult neurogenesis and neuronal regeneration in the central nervous system of teleost fish. Brain Behav Evol 58:250–275.

Zupanc GKH (2001b) A comparative approach towards the understanding of adult neurogenesis. Brain Behav Evol 58:246–249.

Zupanc GKH, Hinsch K, Gage FH (2005) Proliferation, migration, neuronal differentiation, and long-term survival of new cells in the adult zebrafish brain. J Comp Neurol 488:290–319.

Zupanc GKH (2006) Neurogenesis and neuronal regeneration in the adult fish brain. J Comp Physiol A 192:649–670.