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Interactions between environmental changes and brain plasticity in birds

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ABSTRACT

Neurogenesis and neuronal recruitment occur in many vertebrates, including humans. Most of the new neurons die before reaching their destination. Those which survive migrate to various brain regions, replace older ones and connect to existing circuits. Evidence suggests that this replacement is related to acquisition of new information. Therefore, neuronal replacement can be seen as a form of brain plasticity that enables organisms to adjust to environmental changes. However, direct evidence of a causal link between replacement and learning remains elusive.

Our hypothesis is that increased neuronal recruitment is associated with increase in memory load. Moreover, since neuronal recruitment is part of a turnover process, we assume that the same conditions that favor survival of some neurons induce the death of others. I present studies that investigated the effect of various behaviors and environmental conditions (food-hoarding, social change, reproductive cycle) on neuronal recruitment and survival in adult avian brains, and discuss how these phenomena relate to the life of animals. I offer a frame and rationale for comparing neuronal replacement in the adult brain, in order to uncover the pressures, rules, and mechanisms that govern its constant rejuvenation. The review emphasizes the importance of using various approaches (behavioral, anatomical, cellular and hormonal) in neuroethological research, and the need to study natural populations, in order to fully understand how neurogenesis and neuronal replacement contribute to life of animals. Finally, the review indicates to future directions and ends with the hope that a better understanding of adult neuronal replacement will lead to medical applications.

1. Neurogenesis and new neuronal recruitment in adulthood

Neurogenesis (production of new neurons) was traditionally believed to occur only during embryonic stages in mammals (Ramon y Cajal, 1913). This phenomenon was first recorded in the adult mammalian brain as well only a few decades ago (Altman, 1962, 1963), but generally treated with skepticism. Today it is widely accepted and is known to occur in the ventricular zone (VZ) of adult brains of many vertebrates, such as birds (e.g., Alvarez-Bullya et al., 1994; Nottebohm, 1985) and mammals, including humans (Alvarez-Buylla and Gracia-Verdugo, 2002; Dayer et al., 2005; Eriksson et al., 1998; Gage, 2002; Gould and Gross, 2002; Rakic, 2002; Sanai et al., 2004). Forty years after its discovery, the process and regulation of neurogenesis is better understood: in birds, most of the new neurons die while migrating (Alvarez-Bullya and Nottebohm, 1988). Those that survive migrate from the VZ to various brain regions, replace older ones and connect to existing circuits (Paton and Nottebohm, 1984; van Praag et al., 2002). In the adult mammalian brain there is a net gain in neuron numbers (Ninkovic et al., 2007), whereas in the avian brain young neurons replace older ones (e.g., Kirn and Nottebohm, 1993; Kirn et al., 1994; Scharff et al., 2000). Adult neurogenesis is a dynamic process and extensive studies have recently shown that its various stages and final outcome are regulated by a wide range of both intrinsic and extrinsic factors, such as hormonal cycles, neurotransmitters, growth and transcription factors, aging, nutrition, physical exercise and living conditions. A few excellent reviews summarize these aspects (e.g., Fuchs and Gould, 2000; Gould and Gross, 2002; Ming and Song, 2005; Rakic, 2002).

As to the possible role of adult neurogenesis, it has been suggested that permanent changes in gene expression encode long-term memories, such that acquisition of these memories is like a final and irreversible step in cell differentiation (Nottebohm, 1984). If so, then the entire neuron, not only the synapse, is the unit of learning (Nottebohm, 1989), and the number of neurons available for storing new long-term memories would be inversely related to the number of prior memories acquired. For animals such as birds, with a relatively long life span, memory space could run out well before normal life expectancy. A solution would be to replace old neurons and the memories they held, by new ones, which are not yet committed to a specific task. And indeed, unlike in mammals, neurogenesis and neuronal replacement is particularly robust in adult birds because new neurons are added into much of the telencephalon. Since addition is accompanied by neuron loss, the hypothesis is that changes in information load will be

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associated with an increased replacement of existing neurons by new ones. This prediction has been supported by previous observations, such as of end of summer/early fall waves of neuronal recruitment in the vocal nucleus HVC of adult canaries (Kirn et al., 1994) and in the hippocampal complex (HC) of black-capped chickadees (Barnea and Nottebohm, 1994). The former learn new song and the latter engage in food caching.

Such, and more recent examples, also in mammals (reviewed in Ming and Song, 2005) suggest that neurogenesis and new neuronal replacement are related to acquisition of new information. Moreover, as indicated above, it has been shown that various environmental factors affect the rate of proliferation of new neurons, as well as their survival (reviews by Gould and Gross, 2002; Kempermann, 2002; Nottebohm, 2002; Sandeman and Sandeman, 2000). It is important to note that neurogenesis and neuronal replacement are two different phenomena. Clearly, for the latter to occur, the former must as well. On the other hand, there can be neurogenesis without neuronal replacement. In any case, these two phenomena are regarded as forms of brain plasticity that enable organisms to adjust to their changing environment. Substantial direct evidence of a causal link between neurogenesis and/or neuronal replacement and learning is still needed, but recent studies (such as Snyder et al., 2005; Imayoshi et al., 2008) now suggest that adult neurogenesis plays a role in the formation of some long-term memories. However, we still know relatively little about conditions that influence these phenomena and how they relate to the life of free-ranging animals. In addition, most of these conditions were studied in a single or very few species. Moreover, the functional significance of new neurons in adult brains has also been questioned (Leuner et al., 2006). Hence, additional research is needed to test the effect of environmental conditions on multiple species, to yield consistent results. Nevertheless, the evolutionary conservation of adult neurogenesis suggests that it is of fundamental biological importance, and our current knowledge, albeit incomplete, is sufficient to recognize these processes as realistic contributors to cognitive function (e.g., reviewed in Kempermann et al., 2004).

2. Effects of environmental conditions on new neuronal recruitment, survival, and replacement

This review focuses on neuronal replacement in the adult avian brain and summarizes results from several studies that we carried out during the last decade. Our main goal is to understand the regulation of new neuronal recruitment, survival and replacement in the adult brain, and the significance of these processes to brain function, learning, memory, and behavior. To do so, we try to uncover variables that determine what, when and to what degree animals can learn, and where new information is stored. The main hypothesis is that an increase in new neuron recruitment is associated with expected or actual increase in memory load, particularly in parts of the brain that process and perhaps store this new information. Accordingly, we try to understand how brains encode learned behaviors, how this process comes about, and what benefits it confers to the animal. In this review I will try to present the rationale which guided some of our studies, in order to provide an overview of our current knowledge and put it in a general framework, from which we can hopefully draw general conclusions and suggest future directions.

2.1. Seasonal patterns of food hoarding and new neuronal recruitment

To test the hypothesis that an increase in neuronal recruitment is associated with an increase in memory load, we first focused on black-capped chickadees (Parus atricapillus), common North-American songbirds, which store seeds seasonally: in the fall their diet shifts from insects to seeds that they store within their home range, one item per storing site, hundreds per day. In addition, at this time of the year black-capped chickadees face other changes in their life style that can be inferred to generate an acute need for new spatial memories. Retrieval of stored food and adjusting to the changing environment require that each bird have an updated map of its home range and that it remembers where it stored its caches. We looked at brains of free-ranging adult chickadees at different times of year, and focused on the hippocampus (HC), a brain region that is important in spatial learning (Krebs et al., 1989; Sherry and Vaccarino, 1989). The results (Barnea and Nottebohm, 1994) supported our hypothesis, by showing that an increase in new HC neurons coincided with the time when there was a sharp increase in food-storing behavior and when other environmental changes occurred. The study also compared wild and captive birds and found significantly lower neuronal recruitment in the HC of the latter, indicating the importance of performing research under natural conditions. Another comparison, between adult and juvenile chickadees, found that the HC of juveniles recruited more new neurons than that of adults, perhaps because juveniles encounter greater environment novelty than adults and the larger number of new HC neurons allows them to learn more than adults (Barnea and Nottebohm, 1996). Taken together, these early studies offered us a framework and a rationale for comparing neuronal replacement in additional systems, and to further uncover the pressures, rules, and mechanisms that govern the constant rejuvenation of the adult brain.

2.2. Social environment affects new neuronal recruitment

A later study (Lipkind et al., 2002) tested the effect of another environmental factor – social setting – on recruitment of new neurons in brains of another species – the zebra finch (*Taeniopygia guttata*). These Australian birds are highly social and in nature often move between colonies (Zann, 1996). Therefore social changes are probably a real variable for them, as they acquire significant amounts of novel social information during adulthood. Adult males and females were introduced to environments that differed in social complexity. We found that 40 days after the social manipulation more new neurons were recruited into relevant brain regions of birds that were placed in a complex social setting than in those of birds that were kept singly or as pairs. One of these brain regions was nidopallium caudale (NC), which is known to process auditory and somatosensory information (Funke, 1989; Vates et al., 1996). Zebra finches recognize each other by vocalization (Zann, 1996) and therefore we suggested that regulation of new neuronal recruitment by extent of circuit use might be a general mechanism for ensuring that neuronal replacement is closely attuned to environmental changes. The study also suggested that increases in new neuron numbers were preceded or accompanied by a matching demise of older ones. A follow-up behavioral study (Adar et al., 2008a) showed that the increase in neuronal recruitment under complex social conditions correlated with processing and storing of new information (auditory input; songs the bird hears), but not with auditory output (songs produced by the bird).

2.3. Social environment affects new neuronal survival

Next, we extended our observations by asking how social setting, brain region and time from social change affect new neuronal survival (Barnea et al., 2006). The results indicated that factors that promote survival of new neurons also promote the death of older ones, that the rate of neuronal turnover is region-dependent, and that neurons survive differentially in different parts of the same brain region (NC). Some of these results are presented in Fig. 1. Based on these findings we proposed a new theory, which suggests

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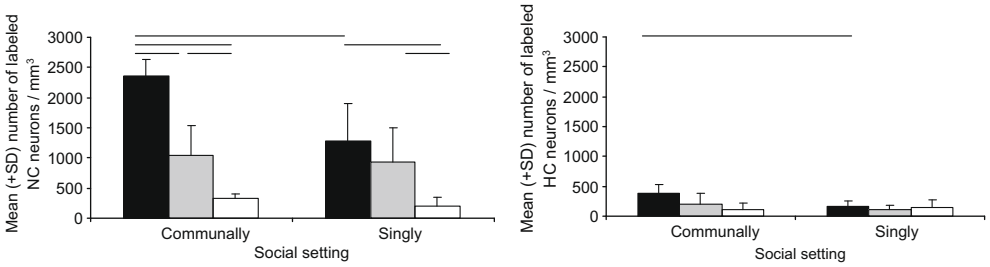

Fig. 1. This figure demonstrates some effects that social environment has on new neuronal recruitment in two brain regions of adult zebra finches: nidopallium caudale (NC) and the hippocampal complex (HC). It presents mean density (neurons per mm^3 ± SD) of new neurons (labeled with the birth marker ^{3}H-thymidine) in the NC (left panel) and HC (right panel), after the exposure of experimental birds to either a new complex social setting (housed with 45 unfamiliar birds), or to a simple one (housed by themselves). Counts of new neurons were made 40 (black bars), 60 (grey bars) and 150 (white bars) days after the social manipulation. Horizontal lines above columns indicate significant differences between groups ($P \leqslant 0.05$). Adapted from Barnea et al., 2006. A few points can be indicated: (A) in both brain regions, at 40 days after treatment, the number of new neurons was higher in communally housed birds than in birds housed singly, suggesting that complex social conditions positively affect neuronal recruitment. (B) In NC, neuronal turnover occurred in both social settings, but it was more marked and significant in the communally housed birds than in the singly housed ones. This suggests that social environment affects neuronal survival. (C) Recruitment of new neurons was higher in NC than in HC, and neuronal turnover was faster and more significant in NC than in HC. Taken together, these findings suggest that different parts of the brain upgrade memories at different time intervals, yielding an anatomical representation of time in the brain.

that different parts of the brain upgrade memories at different time intervals, yielding an anatomical representation of time in the brain. Much as different kinds of sensory information have different anatomical representations in the forebrain, so too, perhaps, has calendar time. If one accepts the possibility that forebrain neurons encode or store information that is acquired by experience, and if one extends this possibility to new neurons, then one form of time representation would be how long neurons that encode change survive. When these neurons are winnowed any information they might have stored will be winnowed too. Since in some brain regions (e.g., NC) the reduction of new neuron numbers occurs faster than in others (e.g., HC), we suggested that the rate at which information acquired by new neurons is lost differs between regions, thus resulting in an anatomical representation of the past. We further hypothesized that those parts of the brain where neuronal replacement occurs at a brisk pace encode recent events, while parts of the brain where replacement occurs at a slower pace or not at all hold older memories. We believe that this novel idea could offer a new way of looking at the brain, one that adds a time dimension to existing maps of function.

A similar approach was taken in a recent study that examined the interactions between social change, age of new neurons, and their position within a brain region (Adar et al., 2008b). We found that exposing a bird to novel social complexity promoted the survival of younger (1 month old) NC neurons and the demise of older ones (3-month old); a less marked social change promoted the survival of older neurons (Fig. 2A). These effects were position dependent within the NC (Fig. 2B). Taken together, the results suggest that brains 'use' exquisite calculations in their 'decision' of which cells to replace and which to keep, under what circumstances and for how long. We believe that this idea can lay out a hypothetical choreography and rationale for neuronal replacement: while older replaceable neurons must be eliminated as the animal grapples with a surge of new information, younger new neurons respond to the same surge as a positive stimulus for their survival. This response remains the brain's most radical way to respond to acute changes in the amount and novelty of information it must process and perhaps, remember.

2.4. Reproductive cycle and new neuronal recruitment

A different behavior, parent-offspring recognition, is another example of learning and memory: in a colonial species like the zebra finch, young fledge from the nest when they still need parental feeding and might easily get lost among other fledglings in the colony. Therefore, it is reasonable to assume that recognition of young by their parents is needed to provide selective parental care (Zann, 1996). Our prediction that this need will be preceded by an increase in neuronal recruitment in relevant parts of the parents' brains was tested and confirmed (Barkan et al., 2007). We observed an increase in new neuron recruitment in the NC, a brain region which is involved in sound processing in the parents' brains and therefore is likely to play a role in auditory parent-offspring recognition. This increase coincided with the need to memorize vocalizations of nestlings before they fledge and was followed by a significant decrease when the young reached independence.

Since our data did not address the issue of whether the changes in NC neuronal recruitment were specific to this region or occurred in all parts of the forebrain where neuronal recruitment was in evidence, we wanted to look at another brain region. For this we chose the olfactory bulb (OB), a region that might also be involved in communication, albeit not auditory. The results from the two brain regions differed: the pattern which we observed in the NC was not found in the OB, suggesting anatomical specificity for the effect seen in the NC.

We also found a preliminary, positive correlation between number of fledglings and number of new NC neurons in the parents' brain at fledging, suggesting that the number of neurons recruited is also sensitive to the number of young fledged.

Recently, we carried out two follow-up studies, which added hormonal and behavioral dimensions to the story: the first (Pnini et al., in preparation) found that prolactin levels in the blood of both parents were highest at hatching. This peak preceded by 3–4 weeks the increase in neuronal recruitment. In mammals there is evidence that high prolactin levels increase neuronal survival (Shingo et al., 2003). It is also known that in the avian brain, 3 weeks are required for neuronal migration from the birthplace to a target region (Kirn et al., 1999). Taken together, we suggest a temporal and functional correlation between prolactin levels and neuronal recruitment, so that high prolactin levels positively affect neuronal recruitment and survival in the avian brain. Another follow-up study provided evidence that zebra finch parents can recognize young that grew in their nest and provide them with selective parental care after fledging (Pnini et al., 2007).

3. General remarks and conclusions

Our studies try to unravel the interplay between brain and behavior. The results indicate a common denominator: when we

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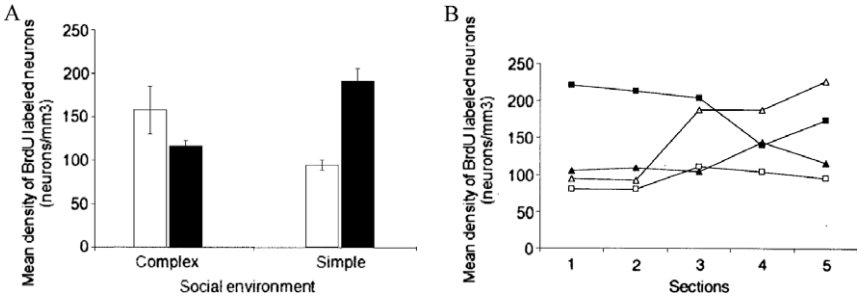

Fig. 2. This figure demonstrates some of the interactions between social change, age of new neurons, and their position within nidopallium caudale (NC), in brains of adult zebra finches. It presents mean density (neurons per mm^3 ± SE) of new NC neurons (labeled with the birth marker BrdU), in brains of males that were exposed to a complex environment (housed with 45 unfamiliar birds) or to a simple one (housed with one unfamiliar female). Taken from Adar et al., 2008b. Two points can be indicated: (A) social manipulation was done when new neurons were 1 month old (white bars), or 3-month old (black bars). The figure shows the interaction between social setting and neuronal age: greater social complexity promoted the survival of younger neurons and the demise of older ones; introducing birds to a simple social environment promoted the survival of older neurons. (B) Birds were exposed to several manipulations: new neurons were 1 month old when birds were introduced to a new complex social setting (Δ) or to a simple one (□); new neurons were 3 months old when birds were exposed to a complex social setting (▲) or to a simple one (■). Density of labeled neurons is shown in each of the five sections sampled along the NC rostrocaudal axis (Section 1 is most rostral). Lines are drawn for descriptive purposes only. This figure shows the interaction between position in NC and social setting: the rostrocaudal position of the section sampled determined, at different neuronal ages, the neuronal survival. This relation applied particularly to birds in the group whose social environment became more complex when the new neurons were 1 month old (Δ). In these birds, complex setting promoted the survival of the young new neurons, and the more so the more caudal the section. This effect was absent when exposure to the complex social environment occurred when the new neurons were 3 months old (▲).

look at a part of the brain that receives new neurons and then look at the conditions that augment the memory load for that part of the brain, the number of new neurons recruited increases markedly as the memory load increases. Moreover, since neuronal recruitment is part of a turnover process, it seems that the very conditions that favor the survival of some neurons induce the death of others. Overall, the results and conclusions from the studies reviewed here draw attention to several general issues that deserve careful examination and consideration in future work in the field of neuroethology.

3.1. Refining terms

Neurogenesis and neuronal recruitment or survival are different processes: the former refers to neuronal birth, which occurs at the VZ; the latter refer to the fate of new neurons, which is determined during their migration from the VZ to various brain regions and at these final destinations. It is important to distinguish between the different events, as has previously been explained and discussed (Nottebohm, 2002; Prickaerts et al., 2004). However, some authors often fail to address this issue. In the mammalian brain, it has already been shown that both neurogenesis and later fate stages (such as survival) can be regulated by various factors (e.g., see the review by Ming and Song, 2005). However, in the case of the avian brain, the yet unproven assumption is that neurogenesis occurs at a constant rate. The available experimental evidence relates only to later stages, and demonstrates the effects that several intrinsic and extrinsic factors have on the migration, recruitment and survival of new neurons. For example, our studies address the effects of various conditions on neuronal recruitment and survival, not on neurogenesis. The question of whether avian neurogenesis is or can be modulated by various factors remains open for future study.

3.2. Refining analysis and discussion of results

Reporting and interpreting results on neuronal recruitment and survival should be performed cautiously and with precision. This is because the interval between the time when the birth marker is given to label the new neurons and the time when the animal is killed might matter a great deal and affect the outcome. Since in the avian brain young neurons replace older ones (Kirn and Nottebohm, 1993; Scharff et al., 2000), the number of new, labeled neurons recorded in a particular study may differ, depending on just when the animal is killed. To complicate matters further, we also know that under the same conditions, the rate of neuronal turnover may differ in different brain regions (e.g., Barnea et al., 2006). Moreover, neuronal survival might also depend on the rostrocaudal position of the recorded neurons within a particular brain region (e.g., Adar et al., 2008b). Taken together, our studies indicate that various factors, such as time from treatment, nature of the experimental manipulation, age of the recorded neurons at the time of the manipulation, and their exact anatomical location in the brain, might interact and affect neuronal survival. Hence, questions about neuronal turnover may have to be informed about such variables. If a study samples a large area and averages the results from all cell ages and locations sampled, real effects might go unnoticed, thus rendering the strategy the brain uses to replace its neurons incomprehensible.

3.3. Distinguishing between predictable and unpredictable factors

It should be noted that some environmental factors that are investigated in relation to their effect on neuronal replacement are 'predictable' ones, while others are not. For example, seasonal food-storing, or particular stages in the breeding cycle are predictable events, because their occurrence is determined by extrinsic and/or intrinsic conditions (e.g., day length, ambient temperatures, blood hormonal levels, etc.). On the other hand, social changes, or number of young that successfully fledge from the nest (out of the total that originally hatched), are 'unpredictable' events that animals have to face and cope with. The relations which we observed between these unpredictable events and neuronal recruitment (Lipkind et al., 2002 and Barkan et al., 2007, respectively) suggest that the brain can respond not only to predictable environmental changes but also to unpredictable ones, which often occur in nature and force the animal to quickly learn to adapt to the new situation and behave accordingly, in order to survive or ensure its offspring's survival.

3.4. Using a variety of approaches and techniques

Neuroethology is an interdisciplinary field of research that examines neuronal mechanisms underlying behavior. As such, it provides an opportunity to explore both proximate and ultimate questions. By combining both levels of analysis (such as behavioral

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and hormonal aspects with anatomical and cellular ones) we might better understand the relations between brain and behavior. To achieve this goal, researchers also need to give close attention to the social and physiological context in which the tested behaviors take place. Studies that incorporate multi techniques and various approaches might uncover the pressures, rules, and mechanisms that govern the brain's constant rejuvenation, offer a framework and rationale for comparing adult neuronal replacement under various conditions, and help to understand its adaptive function.

Our studies often benefit from this combination of the 'whole organism' approach on one hand and from neurobiological aspects, on the other. For example, the neurobiological work on seasonal recruitment of HC neurons in black-capped chickadees (Barnea and Nottebohm, 1994) was accompanied by a behavioral study which looked at patterns of food-storing by these birds (Barnea and Nottebohm, 1995). We found that storing flights ended at short distances from the food source and tended to cluster around a preferred orientation. This orientation often persisted on subsequent days and overlapped that of other flock members. The observed behavior may reflect a compromise between the various needs: to minimize the energy cost of food-storing (close to source), to minimize the risk of thievery (scatter-hoarding), and to optimize the memorization of caching sites. One hypothesis offered to explain this behavior is that cached sites clustered in a particular direction will be remembered with reference to a common set of landmarks, and thus pose less of a memory load than items cached over a broad area in all directions away from a food source.

The benefit of using various approaches when investigating relations between brain and behavior is further demonstrated by our study on the effect of social change on neuronal recruitment in zebra finches (Lipkind et al., 2002), which was accompanied by behavioral observations on the birds' singing behavior after their exposure to the change (Adar et al., 2008a). The latter study indicated that increase in NC neuronal recruitment is correlated with processing and storing of new auditory information.

A third example comes from our work on neuronal recruitment during a reproductive cycle: A behavioral study showed that in zebra finches recognition of young by their parents is needed to provide selective parental care (Pnini et al., 2007). Neurobiological observations confirmed our prediction that this need is preceded by an increase in neuronal recruitment in relevant parts of the parents' brains (Barkan et al., 2007). And finally, hormonal analysis suggested a positive correlation between prolactin levels in the parents' blood and neuronal recruitment in their brains (Pnini et al., in preparation).

3.5. Studying natural populations and more species

Much of the research focuses on laboratory experiments and is, often, 'nature-blind'. Laboratory studies are extremely valuable in increasing our understanding of the basic mechanisms which underlie neurogenesis and neuronal replacement, but it is difficult to extrapolate their findings to the natural world, and thus to determine how neurogenesis benefits animals, including humans, in the struggle for survival. This is especially true in light of indications that captivity affects brain volume (e.g., Smulders et al., 2000) and neuronal recruitment (Barnea and Nottebohm, 1996). Rebored a et al. (1996) already discussed the importance of research in the appropriate behavioral, evolutional and ecological context. They indicated that birds are particularly suited to this purpose, because they show sophisticated and complex forms of memory-based spatial behaviors, including homing, migration, food-storing and, for brood parasitic species, locating hosts' nests. Several years ago, Nottebohm (2002) also advocated that future work on adult neurogenesis and neuronal recruitment should be performed on a diversity of free-ranging animals, because such studies will yield information on evolutionary solutions to a wide range of ecological and behavioral demands.

The need for studies under natural conditions is recognized even by researchers whose work is done in the laboratory. For example, Gould and Gross (2002) write that 'the normal longevity of adult-generated neurons has probably been underestimated by studying animals kept under unnatural conditions'. Promoting studies on natural populations was the aim of a workshop on "Hippocampal neurogenesis in natural populations" held in Toronto in 2000. The consensus of the meeting was that 'demonstration of a role for neurogenesis in natural behaviors will ultimately be essential if we are to understand the purpose and function of neurogenesis'. In a review of this workshop, Boonstra et al. (2001) argue that studies have been unable to determine how the presence of this trait promotes survival and reproductive fitness in the natural world. They refer to the few existing field studies (e.g., our work on free-ranging chickadees; Barnea and Nottebohm 1994, 1996), and express their belief that more such studies will provide fundamental insights into the role and function of neurogenesis. To conclude, I strongly believe that the study of behavior and brain function under natural or naturalistic conditions is an important complement to the study of animals kept in laboratory settings, because many aspects of brain function are likely to be underdeveloped or overlooked in captive animals leading a deprived existence.

Studying natural populations might also increase the diversity of species and environmental conditions which will be tested in association with new neuronal recruitment and survival. This is important because more studies, exploring various conditions and multiple species, are needed to provide consistent results which will help to determine the function of these phenomena.

4. Future directions and overview

Our work on interactions between environmental changes and brain plasticity in birds provided some answers to questions originally asked, but simultaneously opened the door to further investigation. As indicated above, a common assumption regarding the avian brain is that neurogenesis occurs at a constant rate. However, to the best of my knowledge, this assumption has not been tested. Therefore, one of the questions that we are currently exploring is whether adult neurogenesis in birds has a diurnal cycle and whether it is, or can be, modulated by various factors. I hope that such information will shed some light on the yet unknown regulation of neuronal proliferation in the adult avian brain. Other ongoing experiments aim to add new aspects and dimensions to studied systems, and to provide a deeper understanding of the mechanisms underlying neuronal recruitment and survival. One of these experiments aims to support our hypothesis that regulation of neuronal survival is determined by extent of circuit use, by looking at the effect that consecutive social changes (not only one, as we have examined so far) might have on neuronal survival and on the animal's behavior. Another experiment will further investigate the regulation of neuronal survival by testing the hypothesis that prolactin positively affects the survival of new neurons.

An additional study that is currently underway investigates the yet unexplored neuroethological aspects of migratory behavior. This project is being carried out on wild birds, and reflects my strong belief that it is most important to study the relation between behavior and brain function under natural conditions. We compare new neuronal recruitment in brains of closely related migratory and non-migratory birds. The hypothesis is that resident birds face relatively few spatial changes, in comparison with

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migratory birds, which need to process a large amount of new spatial information at least twice a year. The assumption is that the differences in the quantity of new spatial information to which an individual is exposed will be mirrored by differences in the quantity of new neurons recruited into relevant brain regions, such as the HC. The prediction is that new neurons will be recruited into the HC soon after the birds reach their breeding destination and again when they reach their wintering destination, because in both circumstances much new information needs to be acquired. Additional comparisons are made between ages, seasons, and different populations of the same species.

This review presents several studies designed to study brain function by testing the hypothesis that adult neurogenesis and neuronal recruitment serve adaptive functions and contribute to the cellular basis of brain plasticity and to its ability to acquire new long-term memories. These studies use birds as a model and combine behavioral, neuroanatomical and hormonal approaches. By doing so one can benefit from the 'whole organism' approach and create an interdisciplinary study in the field of neuroethology. My hope is that such studies will broaden our knowledge on the regulation of neuronal production, recruitment and replacement in the adult brain and their significance to brain function, learning, memory and behavior. Hopefully, the results will provide better understanding of how brains encode learned behaviors, how this process comes about, and what benefits it confers to the animal.

Finally, neurogenesis and neuronal replacement in adult birds and mammals draw similar conclusions – peaks in information load that must be responded to by behavioral adjustments favor the recruitment of new neurons. This, plus the fact that avian and mammalian brains are sufficiently similar that results will likely be relevant for mammals as well, raises the hope that understanding how neuronal replacement is controlled in birds will lead to future medical applications. I hope that studies that blend basic biology with the aim of better understanding of spontaneous neuronal replacement in healthy adult animals, will enable us to change the way we think about brains and learning, and eventually will be used to repair damaged brains and restore lost functions. Such knowledge might be used to induce neuronal replacement in parts of the brain where it does not normally occur and to make up for cell losses due to injury or disease. In this respect, a concluding remark by Nottebohm (2002) expresses well these thoughts: "Spontaneous neuronal replacement is an improbable brain feature. Before we try our wizardry, we should find out how nature does it."

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