


Review

Artificial Light at Night, Higher Brain Functions and Associated Neuronal Changes: An Avian Perspective

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Simple Summary: Artificial light at night (ALAN) has changed the pattern of natural day–night environment. In recent times, a good amount of focus has been put on the research related with changes in night illumination due to rapid urbanization. In the early 2010s, most behavioural and molecular studies of light at night were focused on nocturnal rodents. However, until recently, songbirds have taken the front seat, as most are diurnal and a highly cognitive species. Artificial light at night (ALAN) affects circadian rhythms in songbirds. Circadian rhythms regulate almost all physiological processes in animals including sleep and cognition. Most of the studies, both in wild and captive birds, have shown negative consequences of ALAN on daily timing, sleep and brain functions. The present review highlights the importance of songbirds as a model for the studies related to light-at-night-induced cognitive deficits. I have also argued and summarized the role of melatonin in ALAN induced changes in sleep and cognition.

Abstract: In recent times, there has been an unprecedented increase in usage of electrical lightning. This has led to increase in artificial light at night (ALAN), and it has been suggested as a source of environmental pollution. ALAN exposure has been reported to be associated with disruption of daily rhythms and serious health consequences, such as immune, metabolic, and cognitive dysfunctions in both birds and mammals. Given the worldwide pervasiveness of ALAN, this research topic is also important from an ecological perspective. In birds, daily timings and appropriate temporal niches are important for fitness and survival. Daily rhythms in a wide array of functions are regulated by the circadian clock(s) and endogenous oscillators present in the body. There is accumulating evidence that exposure to ALAN disrupts clock-regulated daily rhythms and suppresses melatonin and sleep in birds. Circadian clock, melatonin, and sleep regulate avian cognitive performance. However, there is limited research on this topic, and most of the insights on the adverse effects of ALAN on cognitive functions are from behavioural studies. Nevertheless, these results raise an intriguing question about the molecular underpinning of the ALAN-induced negative consequences on brain functions. Further research should be focused on the molecular links between ALAN and cognitive performance, including the role of melatonin, which could shed light on the mechanism by which ALAN exposures lead to negative consequences.

Keywords: artificial light at night; birds; behaviour; brain function; cognition; epigenetics; melatonin; sleep



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1. Introduction

The usage of artificial electrical lightning has led to an increase in artificial light at night (ALAN), and now, ALAN covers more than 80% of the world's inhabited areas [1], which has become a global concern and has recently been asserted as a source of environmental pollution by the American Medical Association. During the last decade, the consequences of ALAN in an ecological aspect, in particular, its effects on avian species, have received great interest [2]. ALAN exposure disrupts the clock-regulated daily patterns of physiology and behaviour and suppresses nocturnal melatonin production [3,4]. Like most organisms, birds have evolved to keep time with the 24 h environmental light–dark cycle, which

is regulated by endogenous circadian clock(s). Daily timings and temporal niches are important for fitness and survival. ALAN exposures have been reported to be associated with serious ecological and health consequences, such as disruption of immune, metabolic, reproductive, and cognitive functions in both birds and mammals [5,6].

Presence of ALAN is a disturbance of the natural habitat, with bright intensity of light close to the light source and low intensity of light at greater distances at night-time, and evidence shows comparable effects of both no-night environment (24 h constant light, LL) and dLAN (dim light at night) in laboratory experiments. There is accumulating evidence that exposure to ALAN regulates and suppresses daily rhythm activity, melatonin, and sleep in birds. Circadian clock, melatonin, and sleep regulate avian cognitive performance. Many studies in wild birds have shown the adverse effects of ALAN on several territorial behaviours, including reproduction, singing, migration, and sleep [7–11]. However, field studies have suggested ALAN increases foraging opportunities in Domestic Pigeon (*Columba livia domestica*) by promoting nocturnal activity and feeding [12] and night foraging in Southern Lapwing (*Vanellus chilensis*) [13]. It is also reported that ALAN allows the Northern Mockingbird (*Mimus polyglottos*) to feed nestlings after dark [14]. Thus, ALAN changes the circadian phase of the feeding behaviour. Further ALAN increases foraging opportunities in nocturnal predatory birds, such as European Nightjars (*Caprimulgus europaeus*) and Burrowing Owl (*Athene cunicularia*), by increasing the abundance of the prey near the light source [15,16]. Thus, modifying the nest-site selection, this might increase vulnerability for the highly specialized birds [13]. Additionally, several laboratory studies have demonstrated the negative effects of ALAN (LL and dLAN) on learning, memory, mood, and exploration [17–19]. Although there is limited research on this topic, most of the insights on the adverse effects of ALAN on cognitive functions are from behavioural studies. Nevertheless, these results raise intriguing question about the molecular underpinning of the ALAN-induced negative consequences on brain functions. Despite clear evidence of potential consequences, how the environmental light signal is translated and induces long-term consequences remains unclear. In this review, I have first outlined the consequences of the ALAN circadian system and sleep, then mainly focused on the effects of ALAN on brain functions and known underlying mechanisms. Thereafter, I have highlighted the possible involvement of melatonin and epigenetic modifications in ALAN-induced responses. The overarching mechanism(s) are general and apply to many different species; however, here, we focused on bird species and discussed the importance of the avian system for better understanding of the subject.

2. Review Methods

I retrieved research articles and reports using Google Scholar for the period between 2006 and 2021 (15 years). Combinations of search phrases that included, ‘light at night + sleep + cognition + brain function’ and words and phrases associated with ‘neuron’ such as ‘light at night + neurogenesis’ or ‘light at night + sleep + cognition + brain function + neurotransmitter’ were used. Further, adding words, ‘light at night + sleep + cognition + neuron + melatonin + birds’ to the search criteria, we finally identified a total of 3420 articles and reports. I reviewed the abstracts or full texts of these articles to further identify articles or reports that have results from studies on avian species. I eliminated the papers that presented no new data related to avian behavioural changes under light at night or presented only perspectives or opinions. I retained the original research articles and reports in the English language, including a few reviews that were used to reach other information sources and retrieve the original articles related to the present topic (see Supplementary Figure S1). Further, expanding the search for ‘epigenetic’ studies on avian species, we could not find reports presenting data on epigenetic modifications in bird species (except [17]); thus, I included a few studies on rodents to make the case for the importance of melatonin and epigenetic modifications underlying neuro-cognitive functions under ALAN (due to similarity in molecular pathways between rodents and birds). Finally, we retained research articles on avian species and included a few of those that were related to studies on

rodents but important for highlighting the critical role of melatonin and epigenetic changes proposed to be involved in light at night induced negative consequences.

3. Artificial Light at Night—Circadian Misalignment and Sleep Disruption

In birds, separate independent circadian oscillators are present in the hypothalamus, retina, and pineal gland, which interact with each other and the periodic environment (e.g., light–dark cycle) to produce timing at the functional level [20]. The environmental light cue is detected by the photoreceptors present in the retinas, pineal gland, and deep brain photoreceptors [20]. Thus, activation of these photoreceptors can alter the expression of clock genes and nocturnal melatonin levels. Exposure to night-time light disrupts the circadian system and desynchronizes the associated behavioural rhythms in both wild and captive birds. In Eurasian Blackbird (*Turdus merula*) and Great Tits (*Parus major*), LAN induced activity in dark phase and nocturnal restlessness was observed [21,22]. Interestingly, the effects of ALAN on activity behaviour have been shown to be intensity and wavelength dependent in Great Tits [11]. Similarly, no-night environment (constant light; LL) and dLAN exposure induced arrhythmicity in the activity and rest pattern and night-time restlessness in captive Zebra Finches (*Taeniopygia guttata*) and House Crows (*Corvus splendens*) [17–19]. The presence of an ALAN environment has been shown to alter the daily singing behaviour in free living songbirds (European Robin (*Erithacus rubecula*), Common Blackbird, Song Thrush (*Turdus philomelos*), Great Tits, Blue tits (*Cyanistes caeruleus*), Common Chaffinch (*Fringilla coelebs*), and American Robins (*Turdus migratorius*)), and similarly in captive songbirds (Zebra Finch) [8,19,23]. ALAN also changes the migratory stopover behaviours of various nocturnal migratory birds [8,9] and negatively affects survival and fitness in birds. Further, it also disrupts the daily rhythms in hormonal secretion, in particular, the release of melatonin [18,19], which plays an important regulatory role in many physiological processes including body mass, metabolism, immunity, and sleep [24].

The temporal organization of daily behaviours is governed by the molecular clock, which functions in a closed transcriptional-translational negative feedback loop and is formed by a set of clock genes [20]. *Clock* (*Circadian locomotor output cycles kaput*) and *bmal1* (*Brain and muscle Arnt-like protein-1*) form the positive limb, and *per* (*Period*) and *cry* (*Cryptochrome*) genes form the negative limb of the molecular clock. Recent evidence suggests that ALAN-induced behavioural and physiological changes are associated with disruption of circadian clock gene expression in birds [25,26]. Zebra Finches born under an LL environment in the laboratory showed differential effects with loss of rhythmicity in the activity and singing behaviour in 30% in males. However, the overall song quality declined [27]. Additionally, there was loss of rhythmic expression of clock genes in the hypothalamus and song nuclei under LL [27]. Similarly, female Zebra Finches born under LL showed loss of rhythmic expression of clock genes in the hypothalamus and peripheral tissues [28]. Further, dLAN affects the expression of *bmal1* in brain, liver, spleen, and blood tissues in Great Tits, along with alteration in metabolic and immune genes [25]. dLAN reduced the peak amplitude of the *per2* gene rhythm, but not *bmal1*, in the hypothalamus of zebra finches. Additionally, dLAN exposure abolished the rhythm in expression of *clock* and *cry1* genes [26]. Further, ALAN impairs metabolism and alters metabolic gene (*sirtuin1*; *sirt1*, *glucose 6-phosphatase*; *g6pc* and *Forkhead box protein O1*; *foxo1*) expression in Zebra Finches [29,30]. Another study demonstrated the effects on diurnal pattern of gene expression of pro-inflammatory (*interleukin-1 β* ; *IL-1 β* , *interleukin-6*; *IL-6*) and anti-inflammatory (*IL-10*) genes in the brain of Zebra Finches [31]. It has also been suggested that urban environment (exposure to ALAN) changes the phase or amplitude of the gene expression rhythm in the hypothalamus, retina, and pineal gland of Eurasian Tree Sparrow (*Passer montanus*) [32].

A critical circadian clock-dependent effect of ALAN might be associated with sleep defects [10,11,18,26,33]. Growing evidence demonstrates that ALAN can influence the total amount, timing, and structure of sleep in many bird species for, e.g., Domestic Pigeons (*Columba livia domestica*), Great Tits, Corvids, and Zebra Finches. Great Tits spent a

significant amount of time awake inside their nest box during night-time in the presence of dLAN compared to the conspecifics in the dark night [10]. dLAN also increased nocturnal vigilance in Indian Peafowl (*Pavo cristatus*) to avoid predators and thus faced a trade-off between vigilance and sleep [33]. Additionally, there was a decrease in resting period and increase in sleep deprivation in House Crows exposed to LL and dLAN [17,18]. Some evidence suggests these changes in sleep behaviour are associated with reduced oxalate, a biomarker of sleep debt, as shown in Great Tits and Zebra Finches [11,26]. In Zebra Finches, ALAN has also been shown to alter the expression of genes associated with sleep [26]. With advancements in technology, recent electroencephalogram (EEG)-based sleep studies have now provided further insights into the effects of ALAN on sleep in birds. Studies have demonstrated that, when exposed to urban intensities of ALAN, sleep in captive Domestic Pigeons and Australian Magpies (*Cracticus tibicen tyrannica*) was reduced with slow-wave activity during non-REM sleep and showed more fragmentation with a lower fraction of REM sleep (out of total sleep) compared to dark night [34]. Together, these results provide behavioural, genomics, and electrophysiological evidence of disrupting effects of ALAN on circadian rhythms, nocturnal melatonin levels, and sleep behaviour. However, it is difficult to pinpoint the causal link between the consequences and ALAN-induced disruption of temporal organization. With several studies suggesting melatonin suppression, pineal melatonin has been proposed to be a possible link mediating the environmental light cues to the brain [3–5,24].

4. Adverse Effects on Cognitive Functions

Circadian disruption and ALAN are implicated in impaired cognition and mood disorders. Many studies have shown the negative effects of LL and dLAN on both cognitive performances and depression in birds [17–19]. Studies on House Crows have provided evidence of declined visuo-spatial learning and memory in presence of LL. The crows were caught in the wild and exposed to LL for 10–14 days in captivity [17]. Thereafter, behavioural rhythms were recorded, and crows were tested for learning and memory tasks. Crows showed impaired spatial and pattern-association learning when exposed to LL, compared to dark nights [17]. At the brain level, there was decreased neuronal activity in the hippocampus (HP) and caudal nidopallium (NC). Further, there was alteration in the midbrain (substantia nigra; SN and ventral tegmental area; VTA) dopaminergic system, as shown by decreased numbers and activity of tyrosine hydroxylase (TH) immunoreactive cells in LL [17]. An LL-induced decrease in TH-positive dopamine neurons has been also shown in rats and implicated in mental disorders [35]. Additionally, an LL-induced decrease in neurogenesis and dendritic complexity of the new-born neurons in the hippocampus and caudal nidopallium has also been shown in House Crows [36]. Similarly, a behavioural experiment on aviary-bred Zebra Finches exposed to LL demonstrated it had detrimental effects on activity and signing rhythms [19,27,28]. In addition, LL induced a decline in advanced brain functions such as learning and personality traits in Zebra Finches (*Taeniopygia guttata*) in adults, and in future generations as well [19]. Similarly, recent study also suggested dLAN negatively affects cognitive performance (novel object exploration and learning and memory) in Zebra Finches [37].

Another study demonstrated that House Crows exposed to dLAN showed depressive-like responses, such as reduced eating and grooming and increased feather-picking and self-mutilation associated with sleep deprivation [18]. Feather-picking and self-mutilation in birds can be considered analogous to trichotillomania (hair-pulling behaviour) in humans and is associated with a depression-like negative state [37,38]. In these crows, dLAN induces changes in hippocampal *bdnf*, *il-1 β* , *tnfr1*, and *nr4a2* expression, and importantly, dLAN affected the histone H3 acetylation at the brain-derived neurotrophic factor (*bdnf*) gene and repressed *bdnf* mRNA expression. dLAN also modulates the expression of the *histone deacetylase-4 (hdac4)* gene in the hippocampus. dLAN reduces neurogenesis in the hippocampus, and it has been suggested that BDNF is involved in decreased hippocampal neurogenesis and the development of depressive-like responses [39]. In contrast to House

Crows, Zebra Finches exposed to dLAN showed decreased neuronal density and therefore a compensatory increase in neurogenesis in the hippocampus [40,41].

Recent research on crows also demonstrated the negative impact of LL and dLAN on brain architecture. LL and dLAN decreased neuronal soma size and glial numbers in the hippocampus and lateral caudal nidopallium [42]. Neuronal soma size and glia-neuron ratios are important for optimal brain functions [42–44]. In humans, reductions in soma size and glial density have been implicated to be associated with reduced cognitive abilities related to depressive mental pathologies [45,46]. Altogether, in addition to behavioural changes, ALAN influences the brain at both structural and functional levels in bird brains, like the results from studies on rodents. For instance, rats exposed to LL showed impaired hippocampal-dependent spatial learning with accompanying changes in long-term depression in hippocampal neurons [47] and decreased neurogenesis [48].

Sleep deprivation is associated with memory deficits, compromised attention and decision-making, and mood disorders in rodents [49–51]. In birds, ALAN-induced sleep deficits and cognitive dysfunctions are shown in House Crows and Zebra Finches. In contrast, Peafowl (*Pavo cristatus*) and Great Tits exposed to ALAN showed sleep disruption but unimpaired cognitive performances [33,52]. Few studies on nocturnal mice showed ALAN-induced depressive behaviour but without any effects on sleep after ALAN exposure [51,53]. A summary of the results from recent studies in different avian species are presented in Table 1. However, the depth of relationship between sleep and cognitive functions is unclear and warrants further research. Nonetheless, as noted earlier, the ALAN effects on brain functions could also be mediated through the hormonal pathway. Melatonin functions as a critical molecule in regulation of brain function either directly or indirectly by altering the circadian rhythm and sleep. Thus, it is pertinent to understand the direct involvement of melatonin in regulation of neuronal plasticity.

Table 1. Summary of the results from recent studies in different avian species highlighting the effects of light at night on behavioural phenotypes and the molecular correlates.

Species	Light Environment	Affected Behavioural Phenotype	Molecular Correlates	Study
American Robins (<i>Turdus migratorius</i>) European Robin (<i>Erithacus rubecula</i>)	ALAN	- Advances the morning chorus into the night		Miller [23]
Eurasian Blackbird (<i>Turdus merula</i>) Song Thrush (<i>Turdus philomelos</i>) Great Tits (<i>Parus major</i>) Blue Tits (<i>Cyanistes caeruleus</i>) Common Chaffinch (<i>Fringilla coelebs</i>)	dLAN	- Alters the phenology of dawn and dusk singing (Earlier in the year than before)		Da Silva et al. [8]
Blackbirds	dLAN (~0.3 lux)	- Early onset of activity and night restlessness		Dominoni and Partecke [22]
Blackbirds	dLAN (~0.3 lux)	- Increase in pre-dawn activity	Decreased nocturnal melatonin levels	Dominoni et al. [54]
Blackbirds	dLAN (~0.3 lux)	- Advances seasonal testicular growth.		Dominoni et al. [55]
Great Tits	dLAN (~1.6 lux)	- Sleep deficits		Raap et al. [10]
Great Tits	Different doses of dLAN (~0.05, 0.15, 0.5, 1.5 or 5 lux)	- Dose-dependent increase in nocturnal activity	Dose-dependent reduction in nocturnal melatonin levels	deJong et al. [23]
Great Tits	dLAN (~8 lux) of different wavelength	- Increase in nocturnal activity - Sleep deficits	Decreased plasma oxalic acid Reduced telomere length (cellular aging) Shift in <i>bmal1</i> expression	Ouyang et al. [11]
Great Tits	dLAN (~0.1, 0.5, 1.5 and 5 lux)	- Advanced wake-up time	Shift in metabolite expressions Desynchronization of metabolic and immune genes	Dominoni et al. [25]
Blue Tits (<i>Cyanistes caeruleus</i>)	dLAN (2 lux)		Affects feather glucocorticoid levels	Dominoni et al. [56]

Table 1. Cont.

Species	Light Environment	Affected Behavioural Phenotype	Molecular Correlates	Study
Indian Peafowl (<i>Pavo cristatus</i>)	dLAN (~0.75 lux)	- Increased nocturnal vigilance - Sleep loss		Yorzinski et al. [33]
European Nightjars (<i>Caprimulgus europaeus</i>)	dLAN	- Increased foraging opportunity - Changes in habitat selection - Increased foraging opportunity		Sierro and Erhardt [15]
Burrowing Owl (<i>Athene cucularia</i>)	dLAN	- Nest habitat selection near light source		Rodríguez et al. [16]
House Crow (<i>Corvus splendens</i>)	LL (~150 lux)	- Activity rhythm disruption - Learning and memory deficits	Reduced neuronal activity in HP and NC Decreased expression of tyrosine hydroxylase in the mid-brain	Taufique and Kumar [17]
House Crow	LL (~150 lux)	- Learning and memory deficits	Decreased neurogenesis and dendritic complexity in HP and NC	Taufique et al. [36]
House Crow	dLAN (~6 lux)	- Increase in nocturnal activity - Sleep deprivation - Depressive-like	Decreased expression of <i>BDNF</i> , <i>IL1β</i> , <i>TNFR1</i> , <i>NR4A2</i> in HPs Increased HDAC4 expression and histone H3 acetylation of <i>BDNF</i> gene in HP	Taufique et al. [18] * Behavioural phenotypes were rescued by elimination of dLAN
House Crow	LL (~150 lux) and dLAN (~6 lux)		Decreased neurogenesis in HP Decreased levels of nocturnal melatonin	Taufique et al. [42]
Zebra Finch (<i>Taeniopygia guttata</i>)	LL (~5 lux)	- Disturbed activity rhythm - Learning deficits - Disrupted activity and singing behaviour (30% of individuals)	Decreased neuronal soma size Reduced glia–neuron ratio	Jha and Kumar [19]
Zebra Finch (male)	LL (~150 lux)	- Decline in song quality, reduced amplitude and song production	Loss of rhythm in the expression of clock genes in hypothalamus	Prabhat et al. [27]
Zebra Finch (female)	LL (~150 lux)	- Fattening, weight gain, and lipid accumulation in the liver	Loss of rhythm in expression of clock genes in hypothalamus and peripheral tissues	Prabhat et al. [28]
Zebra Finch	LL (~400 lux) and dLAN (~3 lux)	-	Loss of melatonin and corticosterone diurnal pattern Altered diurnal pattern of cytokines in the brain	Mishra et al. [31]
Zebra Finch	dLAN (~5 lux)	- Induced night-time feeding and perch-hopping - Sleep deprivation - Learning and memory deficits - Increased neophobia		Prabhat et al. [37]
Zebra Finch	dLAN (~5 lux)	- Sleep deficits	Decreased plasma oxalate levels Decreased <i>thr4</i> , <i>il-b</i> , <i>nos</i> gene expression, and attenuated <i>achm3</i> mRNA levels	Batra et al. [26]
Zebra Finch	dLAN (~5 lux)	- Increased night-time activity - Nocturnal feeding - Body fattening and weight gain	Changes in gene expression of Ca ²⁺ dependent sleep-inducing pathway Increased levels of plasma glucose	Batra et al. [29]
Zebra Finch	LL (~150 lux) and dLAN (~5 lux)	- Body fattening and weight gain - Hepatic lipid accumulation	Decreased levels of thyroxine and triglycerides Altered metabolic genes expression (<i>sirt1</i> , <i>g6pc</i> , and <i>foxo1</i>)	Malik et al. [30] * Phenotype was rescued by <i>Lactobacillus</i> supplement
Zebra Finch	dLAN		Increased neuronal recruitment reduced neuronal density in the hippocampus Decreased nocturnal melatonin levels	Moaraf et al. [40,41]
Domestic Pigeons (<i>Columba livia domestica</i>) and Australian Magpies (<i>Cracticus tibicen tyrannica</i>)	dLAN (~9.6 and 18.89)	- reduced sleep duration and fragmentation - slow-wave activity during non-REM sleep - reduced REM sleep		Aulsebrook et al. [34]

5. Melatonin Induced Modulation of Neuroplasticity

The pineal gland hormone melatonin (N-acetyl-methoxy tryptamine) is produced and secreted under the dark phase (also known as ‘hormone of darkness’) and is involved

in many bodily functions [57,58]. Melatonin synthesized by the pineal gland is released into the third ventricle, from where it is diffused to different regions of the brain and relays environmental light–dark information. Melatonin mediates its functions through signalling pathways coupled to its receptor MT1 and MT2 [58,59]. The mechanism(s) of modulation of neuroplastic changes by melatonin in the hippocampus involves the activation of hippocampal expression of melatonin receptors. Melatonin induces hippocampal cell proliferation [60] and increases neuronal survival [61] in the hippocampus, which is associated with activation of MT1 and MT2 receptors [62]. In addition, melatonin is also involved in regulation of cognitive performances. Melatonin attenuates memory and cognitive deficits due to sleep deprivation in rats [63,64]. Sleep deprivation decreases BDNF and CaMKII expression in the hippocampus, whereas melatonin prevents these changes and improved the cognitive abilities [64]. Melatonin receptors have been shown to be involved in modulation of mood behaviour. Genetic deletion of MT2 but not MT1 receptor induces depressive- and anxiety-like behaviours in mice [59].

Although both nocturnal and diurnal species produce melatonin during the dark phase, laboratory strains of mice (C57bl/6) lack detectable melatonin rhythms completely. Studies performed on mice (undetectable melatonin rhythms) versus Siberian Hamsters and House Crows (robust melatonin rhythm) have reported similar effects of ALAN on mood [15,32,33]. Melatonin production is sensitive to light and ALAN of even very low-intensity exposures, which also suppresses melatonin production in diurnal animals such as birds, fishes, and humans [15,19,55–67]. Additionally, it is important to mention that light plays a different role in diurnal and nocturnal animals; thus, the effect of ALAN might be different with respect to temporal organization of daily behaviours and melatonin rhythms. Further, exogenous melatonin also promotes dendritic maturation and axonogenesis in the hippocampus of mice [60]. There have been reports demonstrating dLAN conditions suppress melatonin and affect neurogenesis in diurnal birds [15,28,39,40]. Plasma melatonin levels have also been shown to be lower in Tree Sparrows from urban environments, compared to rural birds. The results demonstrated that expression of *Aanat*, *Mel1*, and *Mel2* genes in the pineal is disrupted in urban-dwelling Tree Sparrows [28]. Thus, it is proposed that melatonin suppression by ALAN is not the only mechanism but may be an important effector molecule in ALAN-induced effects on neuroplasticity and cognition in diurnal animals, including humans.

6. Melatonin and Epigenetics: A Possible Link to ALAN-Induced Cognitive Dysfunction

Epigenetic modifications include chromatin modifications such as histone methylation, phosphorylation and acetylation, and DNA methylation. Epigenetic modification of gene expression has emerged as an important regulatory mechanism for various functions, including neuronal functions and mental health [67–69]. Modulation of DNA methylation and the expression of several genes, including *Bdnf*, in dentate granule neurons, promote neuronal progenitor cell (NPC) proliferation and new neuron development in a neuronal activity-dependent manner in the adult mouse hippocampus [70]. Similarly, histone acetylation modifications by histone acetyltransferase and histone deacetylases are also involved in neurogenesis [71]. Neurogenesis has been suggested in the regulation of mood, and evidence suggests an association between neurogenesis and depression [15,72].

Melatonin has been shown to modulate epigenetic modifications and gene expressions [73–76]. High melatonin levels induced the expression of histone deacetylase (HDAC) isoforms and histone H3 acetylation in rat hippocampus and mouse C17.2 neural stem cells [73,74]. ALAN-induced decline in *hdac4* expression and alteration of histone acetylation levels in the *bdnf* gene has been implicated in impaired cognitive performance in crows [15]. Similarly, dysregulation of hippocampal *hdac4* expression has been found to be associated with histone acetylation modification and consequent development of depressive-like responses in rats [75]. Further, exogenous melatonin induces the reversal of ALAN-induced DNA hypomethylation in mice [76]. Altogether, the evidence suggest that epigenetic modifications are one of the possible alternative mechanisms for translation of

the light environment–gene interaction, and melatonin might play an important role in the regulation of this mechanism [77].

7. Conclusions and Future Direction

Widespread adoption of electrical lighting and associated light pollution is an increasing problem compromising the temporal organization of biological activities in animals. In birds, there is accumulating behavioural and genomic evidence that suggests ALAN impacts many aspects of behaviour and physiology, including sleep and cognitive performances. Given the evidence for association of disrupted circadian processes and cognitive performance, ALAN could be contributing to learning and memory deficits and depressed mood in individuals through many different circadian regulated pathways (cf. Figure 1). However, such links are scarce and remain to be demonstrated. Importantly, melatonin might be the connecting link between environmental disruption of biological rhythms and the epigenetic molecular machinery, which regulates epigenetic modification of the genes involved in regulation of brain functions. Thus, the relationship between melatonin, epigenetic modification, and brain functions in birds presents a valuable opportunity for research. It is proposed to examine the link between melatonin and epigenetic regulation under ALAN exposures to understand the underpinnings of the processes. This might open opportunities for using melatonin in reversal of ALAN-induced effects on physiology and behaviours, including cognitive functions. Additionally, rather than examining candidate genes, the field should transit toward genome-wide approaches to studying chromatin and DNA modification, shifting the focus to “genomic marks” and “epigenomic signatures”.

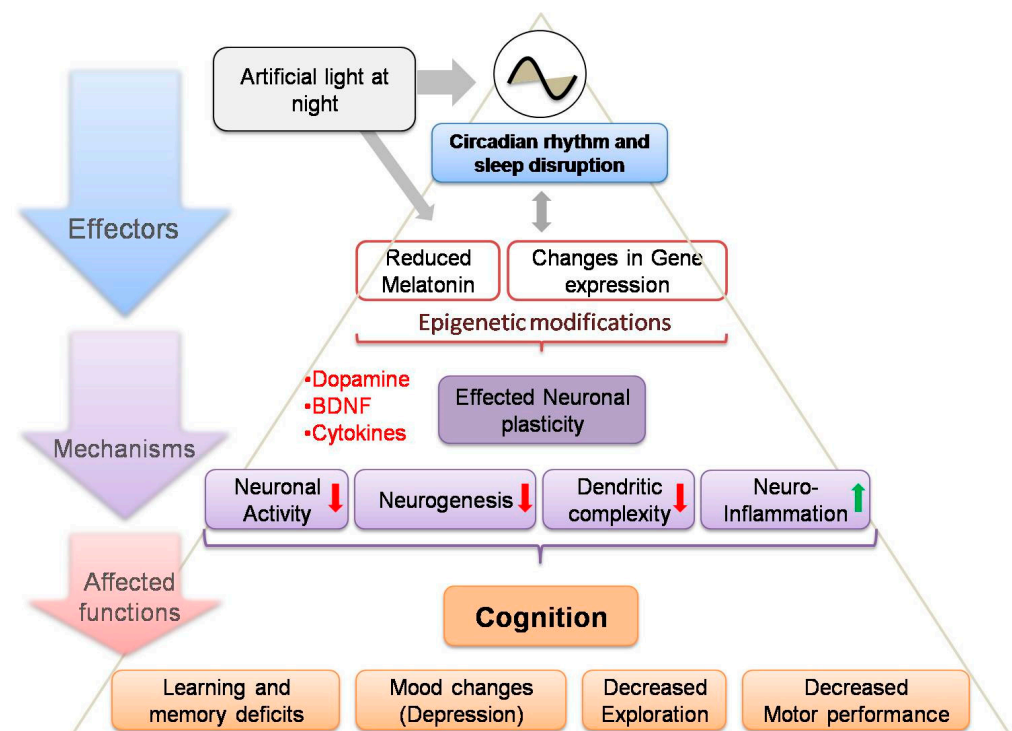


Figure 1. Schematic depicting effect of ALAN exposure, acting on different levels of organization (affectors) via a number of neuronal pathways (mechanisms), those resulting in a series of adverse effects on brain functions (affected functions). This model may help us to understand the complexity of the relationships among exposure components in a systematic manner and may help in assessing the impact on brain functions of ALAN exposure outcomes and their underlying mechanisms (red and green arrows indicate decreased and increased functions, respectively). BDNF: Brain derived neurotropic factor.

Given the unprecedented pervasiveness of artificial light at night worldwide, this research topic is also important from a conservation perspective. While ALAN has been widely documented to have negative impacts on many physiologies and behaviours of individual (free-living and captive) birds, the extent to which this translates to communities and ecosystems is poorly understood. Studies suggest LAN has caused a high mortality in 56 species of seabirds and 298 species of nocturnal migratory birds due to unprecedented attraction to light that leads to grounding or building collisions [78–80]. An estimate of 100 million and 1 billion birds are killed annually in the United States due to building collisions [80]. However, these data are typically fragmentary, biased, and uncertain and can lead to inaccurate impact estimates and a poor understanding of the underlying phenomenon. It is also rather difficult to study the effects of ALAN in wild species in large numbers, and there are limitations with interactions of many other environmental factors. Therefore, a parallel number of laboratory studies are needed to better understand the effects of ALAN on molecular and physiological levels. For these purposes, Zebra Finches would be an excellent model, as they breed in laboratory conditions, and many studies have used zebra finches to understand avian biology, although they are also an outlier amongst the passerine birds [81]. Nevertheless, I believe the most urgently needed actions are to determine a threshold level of light and safe distances from light sources to better understand and mitigate the problems.

Further, the impact on a population is difficult to determine due to the small number of studies that have been conducted, and which are also limited to a few species and/or short-term experiments. To predict the ecological consequences of LAN, it is critical to understand the long-term processes that influence the communities and ecosystem. Although largely unknown, it can be predicted that long term experiments might provide the missing understanding of the response mechanism in the context of evolutionary compensatory mechanisms and impacts on species interactions. To determine the effect of LAN on populations, communities, and ecosystems, it is also important to establish replicated field and laboratory experiments. I also realized there are a few shortcomings in the present literature review, such as search language bias (only English used as criteria for inclusion) and/or failing to discuss the influences of seasonal changes in photoperiod or latitude (where winter photoperiod is very short, and ALAN might provide an increased foraging timing) on mediating the effects of ALAN or the effects of ALAN on behaviour of cathemeral species. Nonetheless, at present, focusing on research investigating the effective mitigation strategies to balance the human need for illumination in society and the needs of darkness for all species is of high importance. As research on this issue continues, small but important global conservation efforts, such as the Fatal Light Awareness Program, Canada (FLAP; <https://flap.org/>, accessed on 8 December 2021) [82], and the Lights Out Program by Audubon Society, USA (<https://www.audubon.org/about>, accessed on 8 December 2021) [83], could help in managing the adverse effects of LAN by advocating the importance of darker night; reducing light pollution and mitigating the problem can be beneficial for all species throughout.

Moreover, research should be focused on field studies on light exposure and the collection of comparative information on different animal models and humans, which would help in understanding the ecological consequences and human health. Additionally, there is a need to develop non-circadian markers measured at multiple time points that could be applied to quantify the extent of the short and long-term effects. Further, conducting acute and chronic repeated experiments on LAN exposure can demonstrate the interactions between hormones, sleep, and metabolism with effects on brain functions. Most of the insights on the adverse effects of LAN on cognitive functions are from studies on nocturnal rodents, and a few are from diurnal species, as mentioned earlier. Additional studies on diurnal animals, for example, birds, should be undertaken to more closely replicate human exposure and the effects thereof and to elucidate the mechanism(s) by which LAN exposures lead to negative consequences.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/birds3010003/s1>, Figure S1: Flow diagram for identification, screening and inclusion of articles and reports from Google Scholar search for the review.

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