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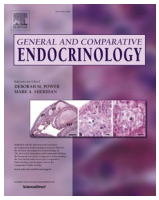

Review article

Impact of artificial light at night and night shift work on brain functions and metabolism☆

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ABSTRACT

The present review focusses on artificial light at night (ALAN) and night shift work (NSW) as examples for chronodisruption occurring in modern societies. Chronodisruption can lead to significant sleep and health problems and increase the risk of chronic diseases. This pathomechanism involves endocrine systems (glucocorticoids, melatonin). ALAN affects at least 80% of mankind and disturbs physiological, biological and behavioral processes in wildlife. In humans, the nighttime use of illuminated screens contributes to ALAN, with as yet unforeseeable consequences for body and brain. Acute continuous light exposure triggers pro-inflammatory responses in the brain which may make it more vulnerable to additional aversive stimuli. Moreover, acute continuous light impairs cognitive function and synaptic plasticity and leads to an increase in corticosterone, a stress hormone and an important mediator in the circadian system. Several studies on NSW reported increased risk for sleep disorders, cancer, cardiovascular disease, type 2 diabetes, obesity, and depression. However, objective imaging analyses supplemented by neuropsychological examinations revealed that NSW has only minor effects on brain functions. Moreover, a recent study showed that NSW was not accompanied by metabolic, cardiovascular or immunological problems. In conclusion, ALAN may be considered a relevant factor influencing human health and biodiversity and should be avoided whenever possible. Studies on the effects of NSW report varying results. This may be due to differences in light intensity during shift, the quality of the occupational health service and the shift work schedule. All these aspects need further investigations to prevent or mitigate the health risk of NSW.

1. Artificial light at night

1.1. General outline

Chronodisruption also called circadian misalignment can lead to impaired mental and physical health (Bara et al., 2023) (impaired cognition, significant sleep and health problems, increasing risks of chronic diseases and cancer). Dysregulation of endocrine systems likely plays a key role in the pathomechanism with glucocorticoids and melatonin being prime targets. This article discusses two examples of chronodisruption that occur in modern societies: artificial light at night (ALAN) and night shift work (NSW). ALAN is considered a real pollutant that can harm people and the environment (Bara et al., 2023).ALAN affects at least 80 % of the world's population and more than 99 % of Europeans. ALAN can disturb physiological, biological and behavioral processes that rely on the natural light cycles in wildlife, plants and marine life. In humans, the nighttime use of illuminated screens, including smartphones, may also contribute to ALAN, with as yet unforeseeable consequences for the body and brain.

1.2. Basics of the circadian system

Living organisms have developed self-sustained circadian clocks that allow them to anticipate rhythmic changes and adapt their behavior and physiology accordingly. The core of the circadian system in mammals is the central circadian rhythm generator in the suprachiasmatic nucleus

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(SCN) of the hypothalamus, also called the conductor of the circadian system. The SCN transmits information to subsidiary oscillators in the brain and body via neuronal and (neuro-) endocrine output pathways. The activity of the SCN is controlled by various input pathways, the most important being the retinohypothalamic tract providing information about the ambient lighting conditions (photoperiod). It controls daily rhythms in brain and body function including the sleep/wake cycle, endocrine rhythms as well as rhythms in core body temperature, detoxification, metabolic and cardiovascular function (Fig. 1). Seasonal rhythms are also controlled by the circadian system. However, their role for human health is investigated only to a limited extent, they play a role in winter depression and are likely involved in the seasonal control of the immune system (Dopico et al., 2015; Korf, 2018; Korf and Moller, 2021).

At the cellular level, the SCN and subsidiary oscillators comprise a molecular clockwork composed of self-sustaining transcriptional/translational feedback loops of clock genes (Reppert and Weaver, 2002) that regulate rhythmic gene expression. The molecular clock drives rhythmic transcription as well as posttranslational (Koike et al., 2012) and epigenetic (Koike et al., 2012) modification and about 43 % of all coding genes and about 1000 noncoding RNAs show circadian rhythms (Zhang et al., 2014; Panda et al., 2002; Akhtar et al., 2002). Because they are self-sustaining, these rhythms also oscillate in vitro with a period length of approximately 24 h (hence circadian). However, most circadian oscillators outside the SCN cease their rhythms in vitro after a few cycles (Duffield et al., 2002), underscoring the importance of rhythmic output signals from the SCN (Akhtar et al., 2002). Moreover, the deletion of the essential clock gene Bmal1 is associated with severe alterations in viability (Kondratov et al., 2006), physiology (Kondratov et al., 2006), cognition (Kondratova et al., 2010), and morphology (Kondratov et al., 2006), including those of the brain (Musiek et al., 2013; Ali et al., 2020) and retina (Storch et al., 2007; Baba et al., 2018; Korkmaz et al., 2025). This underlines the importance of clock genes for maintenance of rhythmic processes and shows that chronodisruption can affect the structure and function of the brain and the light input into the brain.

The SCN controls subsidiary oscillators in the brain through neuronal pathways and neuroendocrine signals, such as SCN-derived AVP. Subsidiary oscillators in the body are controlled by the autonomic nervous system (Buijs et al., 2003) and endocrine pathways (Kalsbeek et al., 2006). Melatonin, also known as “hormone of darkness” and glucocorticoids, also known as “stress hormones,” are important rhythmic signals for circadian oscillators (Balsalobre et al., 2000) in the brain and body. In both nocturnal animals and humans, melatonin levels rise with the onset of darkness, while glucocorticoid levels increase during the late part of the sleep phase and reach peak levels around awakening (Selmaoui and Touitou, 2003; Albers et al., 1985).

Melatonin is produced by the pineal gland under the control of the SCN via the sympathetic nervous system (Korf et al., 1998). It feeds back to the SCN through the G-protein coupled melatonin receptor 1 (MT_1) and 2 (MT_2) (Dubocovich et al., 2003), modulating the amplitude and phase of SCN rhythmicity (Liu et al., 1997). Melatonin synchronizes circadian oscillators subordinate to the SCN (Korf and von Gall, 2006) and drives rhythmic clock gene expression in the pars tuberalis of the pituitary gland (Dardente et al., 2003; von Gall et al., 2005). This is particularly important in the context of the role of melatonin in decoding the length of the night for the control of seasonal rhythms (Korf, 2025). Melatonin is implicated in blood pressure regulation (Pechanova et al., 2014), immune function (Bondy and Campbell, 2020), hippocampal synaptic plasticity and memory processes (Feng et al., 2023), has been proposed as an antioxidant (Reiter et al., 2016) and shown to improve glucose and lipid metabolism, modulate energy balance, attenuate neurodegenerative processes and depressive and anxiety behavior (Korkmaz et al., 2009; Majidinia et al., 2018; Reiter et al., 2010; Repova et al., 2022). In humans and other diurnal animals, melatonin has sleep-inducing capacities because it seems to modulate sleep onset by reducing the threshold for wake-to-sleep transitioning (Kim et al., 2024). Administration of exogenous melatonin affects main characteristics of human sleep, that is, latency to sleep onset, sleep consolidation, slow waves, sleep spindles, and REM sleep (Dijk and Cajochen, 1997). Melatonin produced by the mother and released via the placenta or milk, also represents an important systemic time cue during prenatal and early postnatal development (Verteramo et al., 2022), when the offspring components of the circadian system are not yet fully matured. Importantly, ALAN suppresses melatonin secretion (Lewy et al., 1980) by inducing a rapid decrease in the rate-limiting enzyme in melatonin synthesis (Klein and Weller, 1972).

Glucocorticoid production in the adrenal cortex is under the control of the hypothalamo-pituitary-adrenal axis. In addition, the sympathetic nervous system is implicated in enhancing glucocorticoid production following chronic stress (Lowrance et al., 2016). Glucocorticoids play an important role in energy homeostasis and the circadian rhythm probably serves primarily to anticipate the increase in energy demands associated with wakefulness (Melendez-Fernandez et al., 2023) but is also crucial for the rhythmic function of circadian oscillators subordinate to the SCN (Balsalobre et al., 2000). They are associated with the pathogenesis of lifestyle diseases such as type II diabetes and obesity (Vegiopoulos and Herzig, 2007), with chronodisruption presumably playing a key role (Melendez-Fernandez et al., 2023). Glucocorticoids are also crucial in immune response (Cain and Cidlowski, 2017), cardiovascular (Cruz-Topete et al., 2016; Burford et al., 2017) and reproductive (Whirledge and Cidlowski, 2017) function. Furthermore, glucocorticoids play an important role in the structural synaptic plasticity of the hippocampus (Ikeda et al., 2015) and stress-induced higher glucocorticoid levels impair spatial learning (Krugers et al., 1997). ALAN alters glucocorticoid levels through the involvement of the SCN and the sympathetic nervous system (Ishida et al., 2005), which negatively affects hippocampus-dependent cognitive functions (Ishida et al., 2005). Synthetic glucocorticoids have been used since 1948 in the treatment of immune-related disorders (Cain and Cidlowski, 2017). The widespread role in various physiological systems also explains the diverse adverse side effects of an excess of endogenous or exogenous glucocorticoids (Cain and Cidlowski, 2017).

Melatonin and glucocorticoids have many similarities in terms of their regulation and effects. They also appear to interact in relation to circadian misalignment (Melendez-Fernandez et al., 2023) and stress. In humans, nocturnal physical activity can lead to an increase in cortisol, which precedes a decrease in melatonin, suggesting a temporal relationship between cortisol and melatonin in responses to physical stress (Monteleone et al., 1992).

1.3. The role of light for the circadian system in mammals

Life on earth has evolved under rhythmic environmental changes, such as the 24-hour light–dark cycle and information about the ambient lighting conditions (photoperiod) is the most important environmental stimulus to entrain the circadian rhythm generator in the SCN to the 24 h environmental rhythm.

Light input to brain regions that process non-visual light information, including the SCN, is provided by a subset of intrinsically light-sensitive retinal ganglion cells (ipRGCs) (Hattar et al., 2002; Panda et al., 2002; Ruby et al., 2002; Berson et al., 2002). These not only integrate the light information from the rods and cones, but they also contain an intrinsic photopigment, melanopsin. The ipRGCs use glutamate as a neurotransmitter in combination with neuropeptides such as PACAP (Colwell et al., 2004).

For the SCN, light information serves to adjust the endogenous period length and the phase to external time, a process called photoentrainment (Foster et al., 2020). The circadian clock plays an important role in the interpretation or “gating” of light information for photoentrainment. During the day, light is expected and does not affect the phase of the rhythm generated by the SCN. At night, however, especially at the beginning and end of the night (Foster et al., 2020), light is

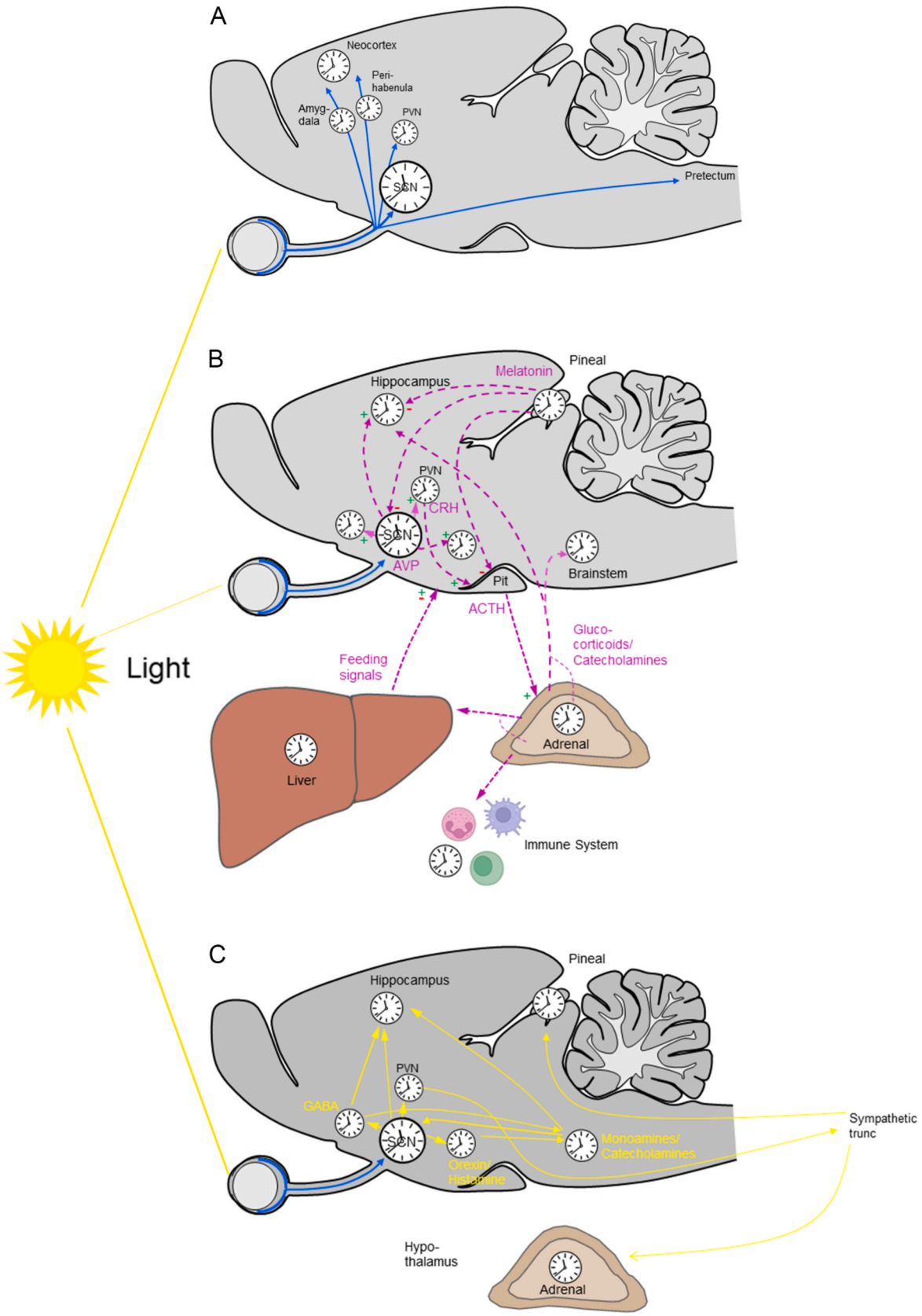

Fig. 1. In mammals including humans ALAN is transmitted via input from the retina. A: Inputs from non-visual photoreceptors into various brain areas, B: (Neuro-) endocrine pathways which are controlled by the non-visual- SCN pathway. C: Neuronal output connections of the non-visual-SCN pathway. All connections may be disturbed by artificial light at night (ALAN). Abbreviations:ACTH adrenocorticotrophic hormone; AVP arginine vasopressin; CRH corticotrophine releasing hormone; PVN paraventricular nucleus; SCN suprachiasmatic nucleus.

interpreted as an error signal, which causes phase shifts of circadian rhythms at the molecular, cellular, and systemic levels (Ginty et al., 1993; Zhang et al., 1996; Gau et al., 2002). In a natural environment, this photoentrainment ensures adaptation to changing light conditions over the seasons. In humans, phase adjustment is particularly evident in the change to daylight saving time and in jet lag, where it typically takes several days for the circadian clock to adjust to the new time.

Photoperiodic signals transmitted from the SCN to key neuroendocrine structures in the brain are also important for the adaptation of physiological processes to the seasons.

In humans, shorter days, thus reduced sunlight, seems to be implicated in winter-onset seasonal affective disorder (wSAD), a type of depression that occurs during the winter and can be mitigated by extending the photoperiod with bright artificial light (Rosentha et al., 1984). In winter, the shorter days and reduced sunlight are thought to affect mood in humans by damping circadian rhythms such as the sleep wake rhythm, and triggering higher levels of the sleep-related hormone melatonin as well as lower levels of serotonin, a neurotransmitter which plays a significant role in mood, behavior, cognitive functions, and the pathogenesis and progression of depression (Shu et al., 2025). Lower sunlight exposure in winter is also associated with a higher light sensitivity of the human circadian system to ALAN in winter (Blume and Munch, 2025).

Non visual light information is provided not only to the SCN, but also directly or indirectly to many other brain regions. Light can therefore influence behavior and physiology on many levels. In nocturnal species, such as the mouse, a widely used model animal in the laboratory, light has opposing effects on behavior, depending on the illuminance, which are known as masking. In dim light, activity is increased compared to complete darkness, which is known as positive masking (Mrosovsky, 1999). In contrast, bright light inhibits activity, which is known as negative masking (Mrosovsky, 1999). Nocturnal animals also prefer dark or dimly lit areas to brightly lit ones. This light aversion is strong enough to counteract the natural tendency to explore a new environment (Crawley and Goodwin, 1980). In contrast, in diurnal species light promotes alertness and vigilance (Foster et al., 2020).

Several brain regions that are related to the circadian pacemaker function of the SCN receive additional direct input from the ipRGCs such as the intergenic leaflet, which provides feedback to the SCN (Moore and Card, 1994), the subparaventricular zone, which plays a role in rhythmic body temperature, sleep and locomotor activity (Vujovic et al., 2015), and the ventrolateral preoptic area and the lateral hypothalamus, which are important for the regulation of sleep and wake (Saper et al., 2005). IpRGCs also control the pupillary light reflex (Hattar et al., 2003) and appear to mediate effects of light on hippocampal long-term potentiation and hippocampus-dependent learning, but this appears to be independent of the circadian pacemaker function of the SCN (Fernandez et al., 2018).

In addition, SCN-independent ipRCGs projections, target the medial amygdala (Luan et al., 2018) and the perihabenula (Fernandez et al., 2018), which are involved in anxiety and affective behavior (LeGates et al., 2014; Schmidt et al., 2011), respectively. The perihabenula, a nucleus of the dorsal thalamus, is connected to the ventromedial prefrontal cortex (vmPFC) as well as the dorsomedial striatum and the nucleus accumbens (Fernandez et al., 2018). Loss of ipRGC signaling in mice leads to dendritic degeneration, dysregulation of genes involved in synaptic plasticity, and reduced neuronal activity in the vmPFC, thereby impairing the ability to regulate emotions (Lazzerini Ospri et al., 2024). It is not yet known whether this ipRGC-dependent influence of light on affective behavior, mood and emotions also plays a role in human mental disorders.

The study by Schroder et al. (Schmidt et al., 2011) suggests that the light/dark cycle rather than rhythmic locomotor activity modulates learning and memory and synaptic plasticity in the hippocampus.

1.4. Detrimental effects of artificial light at night (ALAN)

1.4.1. Humans

In modern society, there is a growing decline in the use of natural light sources such as day-and moonlight and an increase in the use of artificial light sources. Due to artificial lighting conditions indoors and street lighting, people in modern society experience significantly lower illuminance (400–600 lx) during the day as compared with sunlight (~100,000 lx) (Grubisic et al., 2019) and significantly higher illuminance (100–300 lx) in the evening/night as compared with moonlight (0.1–0.3 lx) (Rumanova et al., 2020; Kyba et al., 2017). Due to urbanization and, in particular, the introduction of efficient and cost-effective light-emitting diodes, light pollution has increased rapidly in recent decades (Rumanova et al., 2020). In urban areas, nighttime illuminance reaches 20 lx, locally even 150 lx (Kyba et al., 2014; Gaston et al., 2013). The increase in ALAN disturbs not only the flora and fauna but also humans.

Because ALAN has strong effects on physiological parameters such as hormone secretion, core body temperature, sleep, heart rate, cardiometabolic function and modulates cognitive functions, mood and emotions (Melendez-Fernandez et al., 2023), it could have a detrimental effect on general and mental health in humans. A single night of exposure to room light during sleep can change sleep architecture, heart rate and impair glucose homeostasis, potentially via an increase in the activation of the sympathetic nervous system (Mason et al., 2022). Therefore, avoiding exposure to light at night while sleeping will be beneficial for cardiometabolic health (Mason et al., 2022). Also, as mentioned above, light especially at the beginning and the end of the night shifts circadian rhythms at the molecular, cellular, and systemic levels (Ginty et al., 1993; Zhang et al., 1996; Gau et al., 2002). This means that the later we go to bed and thus expose ourselves to artificial light for longer in the evening, the more we delay our internal clock and thus bed time.

In humans and other mammals (Ganguly et al., 2002) ALAN, particularly light in the blue (460–480 nm) range (Brainard et al., 2001), decreases melatonin synthesis in a time- and dose-dependent manner (Ganguly et al., 2002; Brainard et al., 2001; Rahman et al., 2019). At the same time, ALAN modifies alertness, cardiometabolic function (Mason et al., 2022), vasoconstriction, and heart rate (Cajochen et al., 2005) and leads to an increase in cortisol levels (Rahman et al., 2019). Therefore, ALAN leads to major changes in physiology and two important hormones of the circadian system, promoting a shift from tiredness to wakefulness. Cold light (6500 K), in contrast to warm light (2500 K, 3000 K), in the early night, even at low illuminance (40 lx), can reduce melatonin synthesis and subjective sleepiness and increase alertness (Chellappa et al., 2011). However, there is no convincing experimental proof that blue light screen filters protect children and adults from difficulty falling asleep or hyperactivity when using portable devices in the evening, as claimed by some hardware and software developers. Light suppresses the human SCN activity, as measured by functional MRI (Schoonderwoerd et al., 2022). While blue light (λmax: 470 nm) elicits the highest response, green (λmax: 515 nm) and orange (λmax: 590 nm) light also affect the SCN (Schoonderwoerd et al., 2022). This study shows that the human SCN is sensitive to a broad light spectrum, meaning that all wavelengths of visible light can be potentially disruptive at night. To date, the long-term effects of ALAN, especially on brain development in children and adolescents, have not yet been sufficiently elucidated.

In addition to the general light pollution, light-emitting electronic devices such as televisions, monitors, tablets, and smartphones, which are increasingly used at night, contribute substantially to ALAN (Rumanova et al., 2020; Chinoy et al., 2018). Most portable devices use LEDs that often emit light in the blue wavelength range (Zhang et al., 2023; Campbell et al., 2023), which has the strongest impact on the human SCN (Schoonderwoerd et al., 2022). In particular the use of these devices in the evening close to bedtime negatively affects circadian rhythms in physiology and behavior and sleep (Chinoy et al., 2018). In

the 2011 survey by the National Sleep Foundation, 90 % of US Americans reported using a light-emitting electronic device within one hour of bedtime, with those under 30 more likely to use mobile phones and other interactive devices. The use of interactive devices within one hour of bedtime was associated with difficulty falling asleep and unrefreshing sleep across all age groups (Gradisar et al., 2013). Since the use of interactive smartphone applications and social media, which are particularly popular among young people, have increased significantly since then (Oecd, 2025; Primack and Escobar-Viera, 2017), this is a serious problem. Especially since good sleep is a prerequisite for physical and mental health. Both insufficient sleep and aberrant light exposure (Foster and Wulff, 2005; West and Bechtold, 2015; Wulff et al., 2010) have far-reaching harmful effects on cardiovascular function, metabolism and various brain functions, including attention, mood and cognitive performance (Killgore, 2010). A 2021 *meta*-analysis indicates that an intervention that improves sleep also improves general mental health as well as specific mental health problems such as depression, anxiety, rumination, and stress (Scott et al., 2021). In 2022, 98 % of 15-year-olds and approximately 70 % of around 10-year-olds in the OECD reported having a smartphone with an Internet connection (Oecd, 2025). According to this study, 15-year-olds spend at least three hours on a typical weekday playing video games (27 %) and using social media (63 %) (Oecd, 2025). Although the time of day of use was not recorded in this study, it can be assumed that it primarily occurs in the evening, thus probably affecting both the circadian system and sleep duration. Epidemiologic studies suggest that high social media use (spending two or more hours per day) is associated with conditions such as depression, anxiety, and sleep disturbance, in particular in young adults (Primack and Escobar-Viera, 2017; Shensa et al., 2016). In addition, around 20 % of 15-year-olds reported feeling anxious or nervous at least half the time when they are without their digital devices. Social media users regularly neglected other activities (e.g., hobbies, sports) because they wanted to use social media (Oecd, 2025), indicating signs of addiction. This is also consistent with other studies examining addictive behavior in mobile gaming and social media use among children and adolescents (Westbrook et al., 2021; Burhan., 2020; Pan et al., 2019; Derevensky et al., 2019). The neurotransmitter of the reward system, dopamine, is a potential modulator of the circadian activity rhythm by rewarding stimuli (Tang et al., 2022). The additive effect of light and stimulation of the reward system could explain why the evening use of interactive light-emitting devices has a greater effect on sleep than the use of passive light-emitting electronic devices. However, there are few studies on this topic.

1.4.2. Nocturnal rodents

In the laboratory, exposure of nocturnal rodents, such as mice, hamster, and rats, to constant light (LL) leads to a lengthening of the period and a gradually increasing disruption of circadian rhythms such as rhythms in locomotor activity (Mrosovsky, 2003; Fonken et al., 2010; Ohta et al., 2005) and serum corticosterone levels (Claustrat et al., 2008). In mice, prolonged exposure (7 weeks) to strong or dim constant light leads to changes in the timing of food intake, resulting in excessive weight gain and reduced glucose tolerance (Fonken et al., 2010). LL for three weeks impairs the formation of new neurons, long-term depression in hippocampal neurons, and cognitive performance (Fujioka et al., 2011; Ma et al., 2007), presumably due to stress adaptation (Ma et al., 2007). LL (400 lx) for 14 days, which leads to a prolongation of the period of activity rhythm but not to a loss of rhythmicity, triggers a pro-inflammatory response in the brain which may make it more vulnerable to additional aversive stimuli (Ketelauri et al., 2023). LL (400 lx) for 38 h impairs cognitive function and hippocampal synaptic plasticity and leads to an increase in corticosterone (Schroder et al., 2023). These findings from basic research suggest that ALAN should be avoided, as it causes particularly harmful cardiometabolic and neuronal changes.

Even short exposure to light at the beginning or the end of the subjective night not only leads to a shift in the phase of circadian rhythms and changes in melatonin and cortisol levels but also to major changes in physiology. A one-hour light pulse (100 lx) during the late subjective night and even stronger during the early subjective night leads to an increase in brain and body core temperature, which is probably due to an SCN-mediated increase in sympathetic tone (Song and Rusak, 2000). Similarly, a 30-minute light pulse during the early subjective night leads to altered gene expression in the adrenal gland and to an increase in plasma and brain glucocorticoid levels comparable to that induced by a strong stressor, which appears to be SCN- dependent and mediated by sympathetic innervation (Ishida et al., 2005). These findings suggest that ALAN should be avoided, especially in the early hours of the night, as this is interpreted by the body as a stress signal, leading to physiological changes.

1.4.3. Other ecosystems

ALAN is one of the pollutants emerging with the continued global growth of anthropogenic activities (Bara et al., 2023) and is a threat to biodiversity (Burt et al., 2023; Owens et al., 2020). The detrimental effects of ALAN are not only observed in mammals but also in non-mammalian and invertebrate species and plants which are largely unexplored (Kyba et al., 2014). Since a comprehensive review of the literature on light pollution on other species and plants would go beyond the scope of this article, we refer to the literature database “Artificial Light at Night” (Artificial light at night literature database, xxxx). We would like to give only a few examples that point to commonalities in the harmful effects of ALAN. For example, treatment of toads with continuous light leads to a deterioration in general physical condition, a change in blood count, and an altered response of leukocytes to stress (Gaston et al., 2019), suggesting a general effect of ALAN on stress in vertebrates. Lower concentrations (< 5 lx) of ALAN, which are present in many places as light pollution, probably do not lead to drastic disturbances of the circadian system in vertebrates (Alaasam et al., 2021). However, since the direction, duration, and spectral properties of natural light often serve as a source of information for many organisms about their location, the time of day and year, and the characteristics of their natural environment, ALAN can disrupt this flow of information and provide misleading signals (Kyba et al., 2014). Therefore, light pollution is particularly harmful to migratory organisms such as migratory birds and other species, some of which cross the Earth’s hemisphere (Burt et al., 2023). Moreover, urban songbirds show reduced melatonin secretion and an earlier onset of morning activity than birds kept in dark conditions at night, which is probably due to a misinterpretation of day length (Dominoni et al., 2013). Even weak ALAN (<1.5 lx) appears to alter the behavior and physiology of birds, which is particularly important in the context of light pollution (Alaasam et al., 2021). Furthermore, ALAN appears to be one of the drivers of insect decline, as it negatively affects the development, movement, foraging and reproduction of various insect species and also facilitates prey capture by insectivorous species (Owens et al., 2020). Both local sources of ALAN and diffuse skyglow seem to contribute to the impact of ALAN on physiology, behavior, and fitness of insects (Owens et al., 2020). Light pollution not only directly affects organisms and ecosystems but also interacts and synergizes with other pollutants, resulting in more complex impacts (Pu et al., 2019). For example, patterns of anthropogenic light pollution and ozone pollution are spatially correlated worldwide, suggesting a relationship that needs further investigation (Kyba and A., Hölker, F. , 2014). Transdisciplinary and cross-border approaches to investigating light pollution and its impacts, as well as to mitigating them, are urgently needed to prevent further damage to biodiversity.

2. Night shift work (NSW) and its effects on brain function and cognition

2.1. General outline

Shift work, particularly night shift work (NSW) is another reason for chronodisruption in humans, which potentially affects brain functions and cognition. Consequently, the effects of shift work on brain function and cognitions have been repeatedly investigated, but these studies yielded variable and even controversial results (Kazemi et al., 2016; Hart et al., 2006). A prospective cohort study led to the conclusion that "*shift work chronically impairs cognition, with potentially important safety consequences not only for the individuals concerned, but also for society*" (Marquié et al., 2015). Press media have paid ample attention to this study (Shift work dulls your brain, BBC News, 4 November 2014; Long term shifts ages brains, Sky News, 4 November 2014 https://www.nhs.uk/news/neurology/shift-work-ages-the-brain-study-suggests/). Titova et al. (Titova et al., 2016) showed altered performance in present, but not in former shift workers. Investigations on early career physicians (Alaasam et al., 2021) reported a decline in short-term memory after day and over nightshifts and a high incidence of disturbed sleep, while another study reported that cognitive flexibility during night shifts was not altered per se, but largely depended on the circadian phase of the individual (Cheng et al., 2017). No difference in late-life cognitive aging was observed between individuals with a history of working shifts as compared to those who had typical day work schedules during midlife (Devore et al., 2013).

Cognitive impairment in shift workers may be due to malfunction of brain regions involved in circadian rhythms (Marquié et al., 2015). Circadian misalignment has indeed been discussed to affect neuronal pacemakers (James et al., 2017) and to play a role in psychiatric disorders (Logan and McClung, 2019). Also the individual chronotype, i.e. the intrinsic, biological preference for an early or late sleep onset, is involved in modulation of the functional connectivity (FC) of the large-scale default mode brain network involved in cognitive functions (Facer-Childs et al., 2019). The individual chronotype may also change the ability to cope with shift work (Juda et al., 2013; Griefahn et al., 2002), therefore constituting a potentially important influence. Taken together, alterations within neuronal networks associated with shift work may explain differences in cognitive performance.

Older adults display a high variability in cognitive abilities (Jockwitz et al., 2017; Jockwitz et al., 2017; Jockwitz et al., 2019) which may be influenced up to old ages by various factors (Park and Reuter-Lorenz, 2009; Reuter-Lorenz and Cappell, 2008; Reuter-Lorenz and Lustig, 2005; Reuter-Lorenz and Park, 2010), such as education and lifestyle (Bittner et al., 2019; Bittner et al., 2021). Importantly, cognitive performance as a complex, higher-order brain function involves several brain structural correlates, particularly within the cortex (Burgaleta et al., 2014; Karama et al., 2014; Dickerson et al., 2008). An extensive body of research established the relationship between cortical thickness and cognitive performance in adolescents (Burgaleta et al., 2014; Gennatas et al., 2017), younger and older adults (Frangou et al., 2021) as well as in patients suffering from neurodegenerative disorders (Querbes et al., 2009; Ossenkoppele et al., 2019). Further, cortical thinning has been proposed as a surrogate marker for the early diagnosis of Alzheimer's disease (Querbes et al., 2009). Cognitive decline in ageing and neurodegenerative diseases further affects archicortical structures, such as the hippocampus (Small et al., 1999; Laakso et al., 1995; Dard et al., 2019). A study with flight attendants addressed the problem whether jetlag with short and long recovery periods is associated to volume differences in the right temporal lobe (Cho, 2001). In those with short recovery periods a correlation was found between saliva cortisol levels, lower volume of the right temporal lobe and longer reaction times in a visual-spatial memory task.

2.2. Data obtained from the population-based 1000brains study

2.2.1. Questions and hypotheses

A re-analysis of the 1000BRAINS study (Bittner et al., 2022) allowed to test the hypothesis whether NSW is associated with brain dysfunction by means of **objective** parameters (brain image analyses) and psychological tests (Fig. 2, Table 1) in a large, population-based sample. The participants of the study were divided into three groups: PRESENT shift workers, FORMER shift workers and matched controls (NEVER shift workers). The following questions were addressed:

1. Is there a difference in chronotype between the three groups?
2. Is there a difference in brain parameters between PRESENT shift workers and controls? To this end PRESENT shift workers were compared with NEVER shift workers with regard to (i) resting-state functional connectivity (RSFC), (ii), cortical thickness and (iii) volume of subcortical structures.
3. Is there a difference in brain parameters between FORMER shift workers and NEVER shift workers? This question related to the problem whether the observed differences may be reversible (Marquié et al., 2015).
4. Does longer employment in shift work (measured in number of shift work years) elicit a stronger alteration in brain parameters?

The objective brain image analyses investigations were supplemented by a large set of neuropsychological examinations indicative for performance in several cognitive domains (see Shift work and cognitive performance).

2.2.2. NSW and chronotype

The chronotype has to be considered as a potential modulator between shift work and cognitive performance. Early and late chronotypes are thought to differ in the strength of the circadian misalignment they experience during shift work (Juda et al., 2013). Early chronotypes may cope better with early shifts and late chronotypes may cope better with night shifts: in a cohort of younger participants the chronotype of shift workers was later than in non-shift workers (Schuster et al., 2019). Lower performance in tasks of cognitive flexibility in shift workers was also shown to depend on the circadian phase as measured in saliva-melatonin (Cheng et al., 2017). Furthermore, a recent study on the relationship between chronotypes and RSFC reported fundamental differences in the default mode network (DMN) between early and late chronotypes (Facer-Childs et al., 2019). These differences were considered to account for the compromised attentional performance and increased sleepiness observed in late chronotypes when extrinsic social rhythms do not match their intrinsic circadian phenotype (Facer-Childs et al., 2019). Thus, also misalignment in RSFC of shift workers may depend on their chronotype. However, this possibility can be ruled out in the study by Bittner et al. (Bittner et al., 2022), since there was no difference in chronotype between PRESENT or FORMER shift workers and matched controls.

2.2.3. NSW and resting-state functional connectivity (RSFC)

Resting state functional connectivity (RSFC) derived from magnetic resonance imaging (MRI) was analyzed as a marker for general functional brain architecture and intrinsic communication (Beckmann et al., 2005; Smith et al., 2009). RSFC is associated to cognitive processes, as shown for higher-order cognitive networks (e.g. fronto-parietal, ventral and dorsal attention) and primary processing networks (Stumme et al., 2020) (e.g., the visual and sensorimotor network). Cognitive performance differences seem to largely depend on the communication and cooperation *within* and *between* these functional networks (Stumme et al., 2020; Chan et al., 2014). A highly segregated network that shows high within-network RSFC is considered particularly specialized and effective. On the other hand, highly integrated networks largely depend on other networks and are thus reduced in their specificity. Highly segregated networks may constitute a more resilient functional state against certain types of changes such as circadian disruption by shift

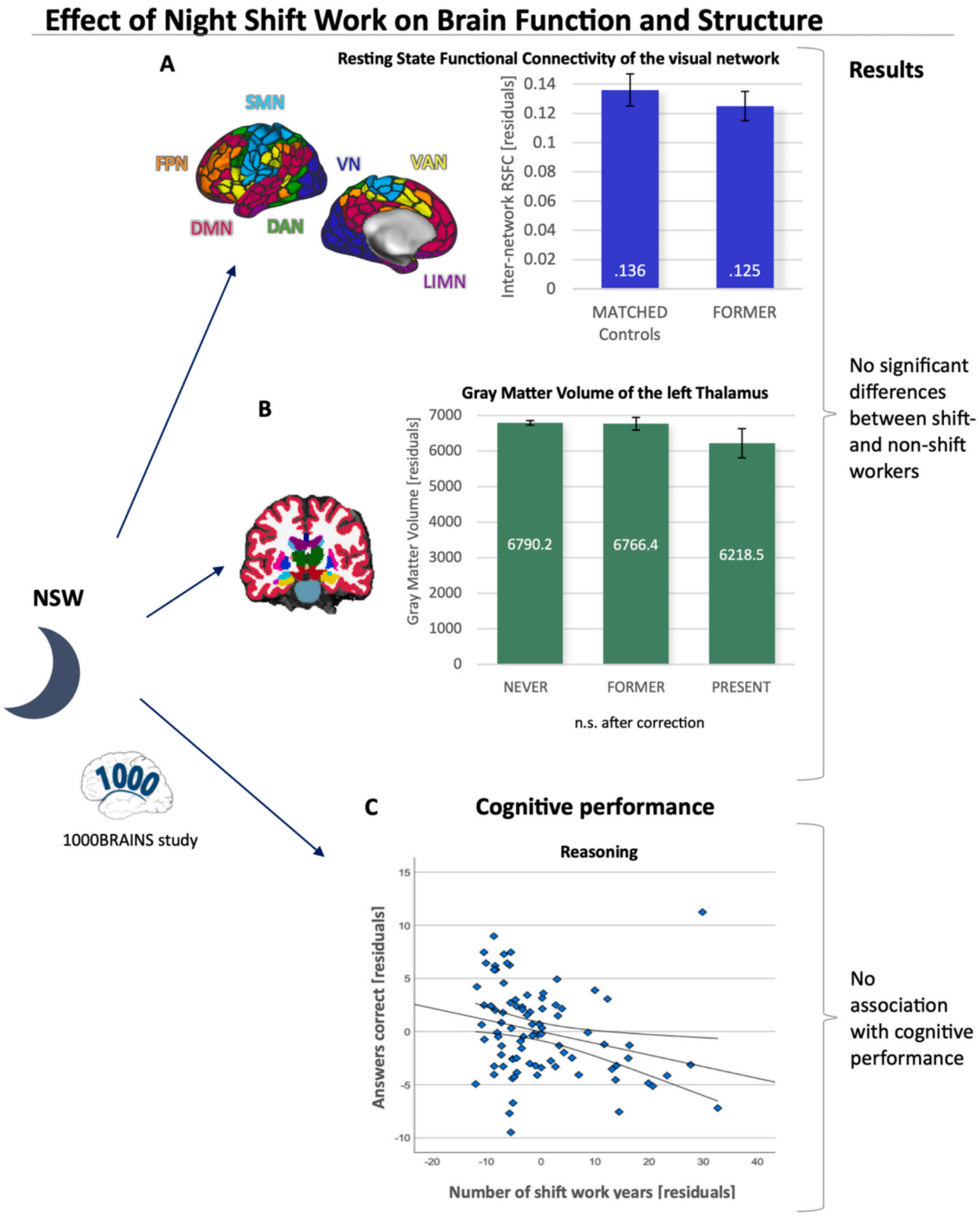

Fig. 2. A: Representation of 7 functional networks on the left lateral surface of the brain: visual network (VN), dorsal attention network (DAN), ventral attention network (VAN), sensori-motor network (SMN), fronto-parietal network (FPN), limbic network (LIMN) and default mode network (DMN). FORMER shift workers showed lower inter-network RSFC of the visual network than MATCHED controls, but these association were not significant (n.s.) after multiple comparison correction. B: Gray matter volume of the left thalamus in PRESENT, FORMER and all NEVER shift workers. None of these association were significant after multiple comparison correction. C: No major effect of number of shift work years on performance in a reasoning task, representative for results obtained in a large neuro-psychological battery. Results are given as residuals since correlations between shift work years and cognitive performance were corrected for age, sex and education. Associations were not significant after multiple comparison correction. Modified after Bittner et al., 2022 (Bittner et al., 2022).

Table 1
Summary of the results from Bittner et al. (Bittner et al., 2022). Abbreviations: FC = functional connectivity; within-FC = functional connectivity between all regions ("nodes") belonging to the same cortical brain network, e.g. visual network (VN); inter-FC = functional connectivity of one network (e.g. VN) to all other 6 networks (sensorimotor network = SMN; fronto-parietal network (FPN), dorsal = DAN and ventral attention network = VAN; limbic network = LIM, default-mode network (DMN)); FCratio = ratio of within-FC to inter-FC for one specific network, thought to reflect integration or segregation of that network.

Parameter	Type of Analysis	Groups	Finding	Details
Analyses of 7 major RSFC networks				
Within-FC, *inter*-FC and FC*ratio* of all 7 major networks	**Group comparison**	PRESENT vs. $NEVER_{PRES}$	No general differences	Small difference in *within*-FC of FPN and FC*ratio* of VN; n.s. after correction
		FORMER vs. $NEVER_{FORM}$	Lower *inter*-FC of VN in FORMER	Effect smaller than in PRESENT shift workers; n.s. after correction
	Correlation with shift years	PRESENT shift workers	Positive correlation with FC*ratio* of VN	More years of shift work → stronger segregation, less FC to other networks; n. s. after correction
		FORMER shift workers	No relationship	
Analyses of brain morphology				
Cortical thickness	**Group comparison**	PRESENT vs. $NEVER_{PRES}$	No differences	No evidence for morphological differences related to shift work
		FORMER vs. $NEVER_{FORM}$	No differences	No evidence for morphological differences related to shift work
	Correlation with shift years	PRESENT	No relationship	
		FORMER	No relationship	
Gray matter volume of subcortical volumes	**Group comparison**	PRESENT < $NEVER_{PRES}$; PRESENT < FORMER	PRESENT: lower volume in left thalamus	No differences in other regions; n. s. after correction
	Correlation with shift years	PRESENT and FORMER	Positive correlation with volume of left thalamus	Longer shift work years →smaller gray matter in left thalamus Also significant after adding total gray matter volume

work, aging or neurodegenerative disease (Wig, 2017; Ewers et al., 2021). The explanatory power of network-wise RSFC for cognitive performance has already been shown within a subsample 1000BRAINS cohort (Stumme et al., 2020).

The analyses of RSFC of 7 major networks of the brain (Stumme et al., 2020; Schaefer et al., 2018) revealed no differences in the executive, attention and default-mode network between PRESENT and FORMER night shift workers and controls (NEVER shift workers, Fig. 2A). However, a strong correlation between more years of shift work and a higher segregation of the visual network was observed in PRESENT shift workers. Thus, the longer the PRESENT shift workers had worked in shift the more segregated the visual network was.

This hints at a reorganization of the connectedness of the visual network with more shift work experience: Potentially the visual network responds to differences in visual perception, e.g. different light exposure due to shift work, with stronger intrinsic connectivity and less connectivity to all other networks. This was explicitly true for the RSFC between the visual and the ventral attention network, which was lower with more years of shift. Thus, within the adaptation process of the visual network to differences in perception it seems to communicate less with the ventral attention network during rest, which is involved in directing selective attention processes (Schaefer et al., 2018).

Less segregation, i.e. higher integration of networks has been discussed as a compensational mechanism, with higher coupling being a means of supporting networks affected by structural decline (e.g. during aging) to maintain cognitive functioning (Reuter-Lorenz and Park, 2010; Chan et al., 2014). Thus, one may conclude that there is less compensational effort with more years of shift work experience.

In contrast, high segregation of large-scale networks has been observed in healthy, young adults and related to better cognitive performance, as compared to older adults, who show more integrated network states (Chan et al., 2014). Accordingly, higher integration has largely been interpreted as a dedifferentiation in functional specialization. Segregated networks therefore are considered as independent entities that are highly specialized to subserve certain processes. The ratio of segregation to integration within the brain *at rest* may reflect an optimal state from which dynamic connectivity changes can be initiated to solve a task (Wig, 2017).

Further, more integrated network states are observed at the beginning of learning an unknown task, while continued practice is accompanied by increased segregation of networks (Shine et al., 2016; Bassett et al., 2015). This conforms to the observation that the visual network is more segregated with higher experience in shift work. It may be speculated, that the greater segregation may be an adaptation to the altered exogenous environment, such as light condition (Cordani et al., 2018) and may therefore reflect a more optimal state during rest for shift workers.

One might hypothesize that this optimal resting state reflects a more bottom-up directed processing where the higher order processing of visual input is rather guided by its exogenous characteristics (light conditions) and processed directly within the visual network (as a primary sensory network) without larger modulations through top-down mechanisms driven by e.g., the attentional networks. Whether and how the connectivity profile of the visual network changes dynamically in shift workers during an active state of *task* needs to be elucidated by further studies. Further, it needs to be considered that larger effect sizes are observed in smaller sample sizes, thus it would be desirable to replicate these observations in a larger cohort.

Since there were no correlations between the number of shift work years and cognitive performance in PRESENT shift workers, it is open whether the observed segregation is a supportive adaptation or a maladaptive uncoupling from the other networks and loss of communication.

Lower RSFC of the visual network to all other networks (*inter-network* RFSC) was also observed in FORMER shift workers as compared to matched controls. However, this effect was smaller than in PRESENT shift workers and not associated to the length of shift, since no correlation between years of shift and RSFC in FORMER shift workers was

found. Even though the increased segregation of the visual network in PRESENT shift workers did not survive multiple comparison correction, it was the strongest effect observed by Bittner et al. (Bittner et al., 2022). Even though inter-network and segregation constitute two different parameters, they point at the visual-processing network as potentially interesting target for future studies focusing on the relationship between brain function and shift work. These studies should also consider the time of the day at which the analyses were performed since activation patterns of brain regions belonging to executive, attentional and the default-mode network were shown to be sensitive to time of the day (Marek et al., 2010). Therefore, larger multi-variate studies are now needed to examine the triangular relationship between night shift work, cognitive performance and functional metrics, such as connectivity.

2.2.4. NSW, cortical thickness and thalamic volume

To supplement the analyses of RSFC, Bittner et al. (Bittner et al., 2022) also examined cortical thickness and thalamic volume, particularly since a previous study discussed correlations between brain structure and recovery periods of flight attendants (Cho, 2001). However, there were no differences between PRESENT and FORMER shift workers and matched controls (Fig. 2B). Thus, an association between shift work and brain morphology is not supported by Bittner et al. (Bittner et al., 2022).

2.2.5. NSW and cognitive performance

The objective brain investigations of Bittner et al. (Bittner et al., 2022) were supplemented by a large set of neuropsychological examinations indicative for performance in several cognitive domains. Based on previous literature, special emphasis was placed to the domains of attention, short-term and working memory, processing speed (Titova et al., 2016; Morris et al., 1989), as well as executive functions (Bäumler, 1985; Marek et al., 2010). Aiming for a complete examination, tests shown to be sensible to age-related decline in cognitive domains (Jockwitz et al., 2017; Jockwitz et al., 2017; Jockwitz et al., 2019) including episodic memory, visual-spatial memory, vocabulary, creative thinking and reasoning (Jockwitz et al., 2017; Caspers et al., 2014) were also performed. In order to establish a triangular association between shift work, differences in brain parameters and cognitive performance, correlation and mediation analyses were performed.

PRESENT shift workers showed faster reaction times as compared to matched controls in the Trail-Making-Test, task A, a measure of processing speed, while they showed lower processing times in the switching task of the Trail-Making-Test (task B – A). No correlations with the number of shift work years were found after multiple comparison correction (Fig. 2C).

Previous studies on cognitive performance yielded variable and inconsistent results. Several studies have reported an association between shift work and cognitive performance in varying parameters. After night shift, lower performance in tasks of cognitive flexibility was described, but this depended on the circadian phase determined by measurements of melatonin levels in saliva (Cheng et al., 2017) and was associated to sleepiness. Unfortunately, no control group was included in this study and thus no information was provided whether the overall performance was lower in shift workers than in non-shift workers. The lower performance could also just be related to “usual after work tiredness” and non-shift workers would show the same after work tiredness.

In a large epidemiological study, current shift workers, but not past shift workers, showed slower performance in all three subtasks of the Trail-Making-Test (TMT) than non-shift workers (Titova et al., 2016), which fits with the results from the study by Bittner et al. (Bittner et al., 2022). As reported by Kazemi et al. (Kazemi et al., 2016), night shift workers made more errors, but reaction times in working memory, sustained attention and processing speed measured with the TMT were comparable to day shift workers. Performance of emergency physicians was comparable after overnight shifts and dayshift, but working memory seemed to be slightly impaired after night shift (Machi et al., 2012). Simulated night shifts seem to impair vigilance and cognitive control (Hart et al., 2006). Matchock and Mordkoff (Matchock and Mordkoff, 2009) provided evidence that even within the attention system subprocesses (orienting versus alerting) rely differentially on time of day and chronotype. These studies show that disruptions of the intrinsic circadian rhythm do not affect global cognitive performance, but they are rather associated to specific cognitive processes, as is also suggested by Bittner et al. (Bittner et al., 2022). On the other hand Marquié et al. (Marquié et al., 2015) found worse performance in current shift workers in a global cognitive score. Taken together these studies clearly point toward the complexity of the association between shift work and cognitive performance. This may be attributed to the time, at which cognitive performance is measured, e.g. directly after the end of shift or the shift work schedule. A study investigating shift work in nurses, found slightly impaired cognition in later life only, if they had a shift work history of more than 20 years in comparison to non-shift workers (Devore et al., 2013). Further, the study of Marquié et al. (Marquié et al., 2015) reported lower cognitive performance in shift workers, who had worked more than 10 years in rotating shift. Bittner et al. (Bittner et al., 2022) also found decreases in cognitive performances with a higher number of shift work years. Even though the correlations were not significant after multiple comparison correction and outlier exclusion, it may be inferred that the number shift years has to be considered as a factor influencing cognitive performance.

In summary, none of the associations between shift work and cognitive performance was significant after multiple comparison correction, neither for group differences nor for correlations. Together with the studies of Marquié et al. (Marquié et al., 2015) and Devore et al. (Devore et al., 2013), who also studied former shift workers, this suggests that shift work has no long-term effects on cognitive performance. It has to be considered, though, that the study by Bittner et al. (Bittner et al., 2022) is a pilot study sample drawn from a population-based cohort of older adults. For future studies, it is essential to differentiate between different cognitive parameters and tests administered, time of examination (e.g. directly after exposure) and between different shift work schedules. Further, it would be desirable to monitor cognitive performance closely in night shift workers in relation to different shift schedules, different work tasks (high cognitive versus low cognitive load), occupational type (e.g. chemistry workers versus clinicians), education, as well as longitudinally also over time.

3. Night shift work and metabolism

3.1. General outline

NSW is listed as risk factor for metabolic, cardiovascular and immune malfunctions (Sooriyaarachchi et al., 2022; Vetter et al., 2018; Khosravipour et al., 2021; Shah et al., 2022; Karlsson et al., 2001; Sookoian et al., 2007; Pietroiusti et al., 2010; Nikpour et al., 2019; Lu et al., 2017; Vetter et al., 2015; Zoto et al., 2019). Changes in expression of circadian clock genes and subclinical abnormalities in HbA1c were found in current night shift workers, but not in former night shift workers and individuals who work during daylight hours only (Rizza et al., 2021). A strong relationship between the circadian system and metabolism has also been demonstrated in animal models. Genetic disruption of the circadian clock predisposes rodents to metabolic disease (Rudic et al., 2004; Turek et al., 2005) and exposure to artificial light at night promoted significant metabolic disturbances (Opperhuizen et al., 2017; Karamitri and Jockers, 2019).

Nevertheless, several aspects about the association between night shift work and metabolic malfunctions remain open. Thus, the sex of the shift workers may play an important role and most studies addressing the association between night shift work and metabolic, cardiovascular and immune malfunctions were performed with females (nurses). Interestingly, a study on male railway workers did not show a

significantly increased risk of the metabolic syndrome by long-term night shift work (Dong et al., 2022). Moreover, retrospective studies comparing a large cohort of male night shift workers with non-shift workers in a German chemical company did not provide evidence for a carcinogenic effect of night shift (Yong et al., 2014), an excessive risk of mortality from cancer (Yong et al., 2014) and non-cancer diseases, especially ischemic heart disease (Yong et al., 2014; McNamee et al., 2006) in night shift workers.

3.2. *Data from the population-based Heinz-Nixdorf recall study and the Heinz-Nixdorf-recall multigeneration study*

3.2.1. *Parameters analyzed*

Bittner et al. (Bittner et al., 2025) evaluated the association between night shift work, metabolism, cardiovascular and immune systems from the population-based Heinz-Nixdorf Recall study (Schmermund et al., 2002) and the related Heinz-Nixdorf-recall Multigeneration study (HNR-MGS) (Fig. 3, Table 2). Particular attention was paid to the metabolic syndrome which refers to the clustering of several known cardiovascular risk factors, including insulin resistance, obesity, dyslipidemia, and hypertension. Participants working in night shift were compared with age- and sex-matched controls who never worked in night shift. The following parameters were analyzed: systolic and diastolic blood pressure, body mass index (BMI), waist hip ratio, levels of HbA1c, fasting blood glucose, total HDL and LDL cholesterol, LDL/HDL ratio, triglycerides, uric acid, C-reactive protein, number of erythrocytes and white blood cells. To investigate sex differences, interaction effects between sex and shift work group were calculated. Furthermore, the relationship between all parameters and the length of shift work was analyzed. Finally, it was examined whether shift workers needed more drugs targeting metabolic, cardiovascular, metabolic and immune functions than participants who were never engaged in shift work.

3.2.2. *Results*

The first series of analyses comprised participants without medication and compared PRESENT shift workers (n = 69) with their respective NEVER shift worker controls as well as FORMER shift workers (n = 212) and their respective NEVER shift worker controls, who were matched for age, sex and sample size to the respective shift working group. None of the mean values of the anthropometric and blood parameters differed significantly. Importantly, PRESENT and FORMER shift workers were not compared directly without age adjustment since former shift workers were significantly older. However, a significant interaction effect was observed between shift work and sex for BMI. Female FORMER shift workers showed the lowest BMI as compared to their respective controls (female NEVER shift workers) or male FORMER shift workers and their respective controls (male NEVER shift workers).

The analyses of the association between number of shift work years and metabolism, cardiovascular and immune system parameters in PRESENT shift workers without relevant medication did not reveal any effect of shift work length or any interaction effect with sex. The same held true for FORMER shift workers. Notably, between subject effects indicated a significant interaction with sex, i.e. erythrocyte numbers were lower in males who had worked in shift for longer periods as compared to shift workers in shorter periods, while in females the numbers of erythrocytes were higher when they had worked for longer periods. However, all mean values and standard deviations were in the normal range in both, male and female FORMER shift workers.

The analyses of the medication showed that the number of relevant drugs taken did not differ between PRESENT shift workers and their matched controls or FORMER shift workers and their matched controls. FORMER shift workers as well as their matched controls took more drugs than PRESENT shift workers and matched controls. However, the number of medications was not associated to shift work but highly significantly related to older age. This association between age and number of drugs was not restricted to a specific type of medication, but was generally found for all relevant drugs.

Since FORMER shift workers were significantly older than PRESENT shift workers Bittner et al. (2025) (Bittner et al., 2025) did not compare PRESENT to FORMER shift workers directly. Slightly elevated values for BMI were observed in PRESENT shift workers and in matched controls. Values for BMI were higher in FORMER shift workers, who also showed increased values for total cholesterol, but again a very similar elevation of these values was also observed in the matched controls. Thus, this increase in BMI and total cholesterol is primarily related to age. When comparing shift work groups (PRESENT and FORMER) directly with selected controls and controlling for age, there was no mean difference in BMI which could be specifically attributed to shift work.

PRESENT shift workers had a different portion of males (66,6% males) than NEVER shift workers (42,2%, before matching) and FORMER shift workers (71,7 % males). Since sex had been considered as one influencing factor (Khosravipour et al., 2021), Bittner et al. (Bittner et al., 2025) matched for sex to balance the higher portion of males in shift- versus non-shift-workers. To still be able to investigate the differences between male and female shift-workers, interaction effects within the analyses of covariance were analyzed. The data revealed very few interaction effects between sex and shift work. In PRESENT and matched NEVER shift workers, male participants showed generally

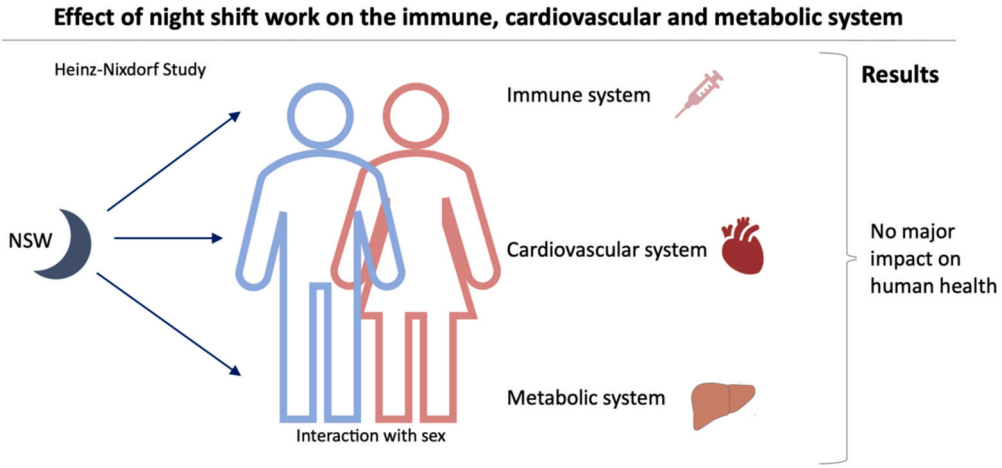

Fig. 3. Effect of night shift work on the immune, cardiovascular and metabolic system as demonstrated in a population-based cohort of the Hinze-Nixdorf Recall and Multi-Generation study (Bittner et al. 2025) (Vetter et al., 2015). None of the parameters examined showed significant differences between shift workers and matched controls after multiple comparison correction. Abbreviations: NSW = night shift work.

Table 2
Summary of the results from Bittner et al. (Bittner et al., 2025). Anthropometric and blood values refer to systolic and diastolic blood pressure, body mass index (BMI), waist hip ratio, levels of HbA1c, fasting blood glucose, total HDL and LDL cholesterol, LDL/HDL ratio, triglycerides, uric acid, C-reactive protein, number of erythrocytes and white blood cells. PRESENT = present shift workers, FORMER = former shift workers, NEVER = all participants, who never worked in shift, $NEVER_{PRES}$ = a subsample of NEVER shift workers, who have been matched in age and sex to PRESENT shift workers; $NEVER_{FORM}$ = a subsample of NEVER shift workers, who have been matched in age and sex to FORMER shift workers; ANCOVA = Analysis of Covariance; MANCOVA = multivariate Analysis of Covariance.

Analysis	Parameters	Groups	Findings
Main analyses			
Group comparison: shift- vs. non-shift workers (MANCOVA)	**Anthropometric & blood parameters, age & sex as covariates**	PRESENT vs. $NEVER_{PRES}$ FORMER vs. $NEVER_{FORM}$	No significant differences No significant differences
Test for interaction between group and sex (MANCOVA)	**Anthropometric & blood parameters, interaction with sex, age as covariate,**	PRESENT vs. $NEVER_{PRES}$ FORMER vs. $NEVER_{FORM}$	Female PRESENT had lowest HDL compared to all groups Female FORMER had lowest BMI compared to all groups
Sensitivity analyses			
Group comparison, including participants with medication (MANCOVA)	**Anthropometric & blood parameters, age & sex as covariates**	PRESENT vs. $NEVER_{PRES}$ FORMER vs. $NEVER_{FORM}$	PRESENT vs. controls: Similar results; additional interactions – females had lowest LDL/HDL ratio and CRP FORMER vs. controls: Similar results as main analyses
Omnibus group comparison using all participants, no matching (MANCOVA)	**Anthropometric & blood parameters, age & sex as covariates**	PRESENT vs FORMER, vs. $NEVER_{all}$	Patterns similar to main analyses; hints at sex-specific triglyceride differences in PRESENT shift workers
Test for group differences in prevalence of clinical values (Chi-square test)	Number of participants beyond clinical cut-offs of anthropometric & blood values	PRESENT vs. $NEVER_{PRES}$ FORMER vs. $NEVER_{FORM}$	Generally, no differences; exception – fewer female PRESENT had HDL levels below cutoff More male FORMER had elevated waist circumference
Analyses of influence of shift work length			
Group comparison: shift workers with short vs. long length (MANCOVA)	Anthropometric & blood values, **age & sex as covariates**	PRESENT vs. $NEVER_{PRES}$ FORMER vs. $NEVER_{FORM}$	No significant effects Interaction in erythrocyte levels: Shift-workers with long history: males had lower levels, females higher levels (but all in normal range)
Analyses of differences in medication			
Group comparison: shift- vs. non-shift workers (ANCOVA)	Number of relevant medications taken	PRESENT vs. $NEVER_{PRES}$ FORMER vs. $NEVER_{FORM}$	No significant differences No significant differences

lower HDL values than female participants, but between male PRESENT and NEVER shift workers HDL levels did not differ. Female PRESENT shift workers showed lower HDL values than female NEVER shift workers within the interaction effect ($p = 0.040$). Thus, HDL levels were significantly different depending on the shift status of women, while this was not true for men. In sensitivity analyses, the differences in HDL between shift workers and controls turned out to be marginal, i.e. female PRESENT shift workers had a mean HDL level of 60.77 mg/dl, while female NEVER shift workers presented a level of 57.35 mg/dl. Thus, both groups presented HDL values above the clinical cut-off value of 40 mg/dl, i.e. both groups presented mean HDL levels in the normal range. Further, the statistical significance has to be considered rather low ($p = 0.04$) and the sample of female shift workers was smaller (n = 23 females) than the male sample and, thus, this difference might be considered as clinically small. However, the interaction analyses emphasized that the differences between males and females seem to be greater in shift workers than in controls for certain parameters or may even be reversed. Hence both sexes should be investigated on their own. Stratifiying for sex, future studies could answer the question whether the effects of shift work depend on sex.

For FORMER and matched NEVER shift workers, there was one significant interaction effect between shift work group and sex for BMI: female FORMER shift workers showed the lowest BMI as compared to female NEVER or male FORMER or NEVER shift workers. Sensitivity analyses no longer showed this interaction, but an interaction with sex was found on levels of HbA1c, where the differences between males and females in shift workers (FORMER) was again greater than in matched controls. Again, female FORMER shift workers showed the lowest levels of HbA1c.

The results by Bittner et al. (Bittner et al., 2025) may therefore suggest small differences between male and female shift workers, but the statistical significance was rather low, as were the effect sizes. When analyzing the proportion of participants with parameter values beyond the normal range a higher percentage of male shift workers with elevated values of BMI, WHR, and glucose was found as compared to female shift workers and controls. Yet, only few of these proportions were statistically significant: One surprising result was that more female NEVER shift workers showed lower HDL-values than female PRESENT shift workers, which might indicate better health conditions for female PRESENT shift workers. For male participants only the higher proportion of FORMER shift workers with larger hip circumference was significant, but not the elevated levels in BMI and glucose levels.

3.2.3. *Synopsis of divergent results*

The observations by Bittner et al. (Bittner et al., 2025) did not provide evidence that night shift work is a major risk for the development of a metabolic syndrome and are in line with results from retrospective studies comparing a large cohort of male night shift workers with non-shift workers which did not provide evidence for a carcinogenic effect of night shift (Yong et al., 2014), an excessive risk of mortality from cancer (Yong et al., 2014) and non-cancer diseases, especially ischemic heart disease (Yong et al., 2014; McNamee et al., 2006) in night shift workers. A systematic review of 12 studies evaluated the cross-sectional association between shift work and the prevalence of metabolic syndrome between day and shift workers, specifically employed in healthcare, with an age range of 18 to 65 years. Like Bittner et al. (Bittner et al., 2025) two studies did not report an association, while ten studies

demonstrated a twofold increase in the chance of developing metabolic syndrome in shift workers as compared with day workers (Sooriyaarachchi et al., 2022). Notably, five of the 12 studies were exclusively conducted in females. The authors suggest that the risk of metabolic syndrome seems to be higher in healthcare workers than in other industries. This might also be related to the high proportion of female nurses examined in the respective studies, or to the irregular shifts in the healthcare sector.

Another systematic review investigated the association between shift work and metabolic syndrome, as well as obesity, dyslipidemia, hypertension, and insulin resistance (Shah et al., 2022). A *meta*-analytic study investigated the cross-sectional association between shift work and metabolic syndrome as well as the roles of sleep, sex, and type of shift work in over 120,000 participants. The pooled Odds ratio of metabolic syndrome in shift-versus day-workers was estimated as 1.14, thus much lower than estimated e.g. by Sooriyaarachchi et al. (Sooriyaarachchi et al., 2022) and was no longer significant when cohort and case-control data were considered. Further, the odds ratio was significantly higher for those studies conducted only on females or males, compared to those in mixed samples, and rotating shift workers had stronger odds of metabolic syndrome than the other shift workers (Khosravipour et al., 2021). The higher prevalence of metabolic syndrome in nurses seems to hint at sex being one important factor within the association to shift work. However, another study in Korean female nurses (Jung et al., 2020) found a higher metabolic syndrome prevalence in non-shift working nurses than in shift working nurses. This is in line with the findings by Bittner et al. (Bittner et al., 2025) that female FORMER shift workers showed a lower BMI and higher HDL-levels as compared to female NEVER shift workers. Further along this line, female PRESENT shift workers also presented the lowest triglyceride levels, compared to male shift workers, but also compared to all other females, who never worked in shift. Hence, these data suggest an interaction effect between sex and shift work group and it might thus be desirable for future studies to model the differences and interactions between females and males more deeply. Specifically female PRESENT shift workers might display a research group of interest. Here, Jung et al. (Jung et al., 2020) argued that their observations might be related to a higher amount of physical activity of shift work nurses, as well as eating habits which can be related to a large proportion of variance in metabolic syndrome in nurses since caloric intake and specifically the number of calories eaten during evening hours explained more variance in metabolic syndrome risk than shift work. In this line, Vetter et al. (Vetter et al., 2015) examined female nurses in a prospective study design, but with a particular focus on shift work schedule, chronotype and type 2 diabetes. There was only slight evidence that newly developed type 2 diabetes was higher in shift working nurses than day working nurses. Moreover, the relation to shift work was much more complex: the proportion of nurses with type 2 diabetes was not elevated in women working less than 10 years in shift work as compared with those working more than 10 years. Among early chronotypes, risk of type 2 diabetes was modestly reduced when working daytime schedules. In contrast, late chronotypes showed a significantly increased diabetes risk in day workers. Interestingly, this was attenuated if their work schedules included night shifts. These observations further hint at a mismatch between work schedule and chronotype which may explain some of the variance in developing type 2 diabetes and may also be considered for metabolic syndrome. In the study by Bittner et al. (Bittner et al., 2025) no sufficient data about the chronotype and the precise shift work schedules were available which, however, need to be addressed in future studies.

4. General conclusions

ALAN may be considered a relevant factor influencing human health and biodiversity and should be avoided whenever possible. Studies investigating the impact of night shift work as a chronodisruptor and general risk factor for human health have yielded equivocal, sometimes even controversial results. Potential explanations for these varying results may be manifold and include inter alia differences in the (i) lighting conditions during shift, (ii) schedule of night shift work (fast rotating versus slowly rotating shifts), (iii) adaptability to shift work (Harding et al., 2024) and (iv) the socio-economic differences, particularly the quality of healthcare provision of study participants. Also, the sleeping behavior and the chronotype may have an impact. All these data need to be recorded in future studies in order to clearly define the impact of night shift work on human health and to implement tailored health care programs to prevent or mitigate significant effects of shift work on human health.

CRediT authorship contribution statement

Horst-Werner Korf: Writing – original draft, Project administration, Investigation, Conceptualization. **Nora Bittner:** Investigation, Methodology. **Svenja Caspers:** Conceptualization, Writing – review & editing. **Charlotte von Gall:** Conceptualization, Writing – original draft.

Data availability

Data will be made available on request.

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