Karl,
This is a draft of part of a chapter I am writing on sleep and the neurological development of children. It deals with immunity and viral infections, thus seems timely. Short take - don't short your sleep time if you want to avoid getting viral diseases.
Charly

Earlier in this chapter, it was pointed out that growth hormone (GH) and prolactin, released during SWS (short wave sleep) are essential to growth and development of neurons and oligodendrocyte precursor cells in the brain. In the brain, glial cells have immune function; immune cells outside of the brain share several intercellular signalling molecules with neurons and glial cells. Some immune modulators can cross the blood brain barrier, and thus share signalling between the CNS and the peripheral immune system.

Short wave sleep supports the adaptive immune response to bacterial and viral infections and as well to cancer. Antigen presenting cells (APC) are immune cells that temporarily reside in different non-CNS tissues in the body, where they keep a watch out for and then take up foreign materials (such as viral or bacterial antigens). The APC then migrate into the lymphatic channels and into the lymph nodes. Here they present the processed antigens to T-helper cells. The T-helper cells then differentiate into the appropriate form appropriate for the type of disease, (i.e, Th1, Th2, Th17 cells) that become specific to the antigen. These Th cells then multiply and regulate the attack against the infection or cancer cells and help promote the formation of antibodies to the antigen. Th1 cells are essential in the immune response against viruses, intracellular bacteria, and cancer cells.

The immune response has a diurnal rhythm. Clock genes, which control which part of the diurnal cycle various proteins are transcribed, control up to 8% of the transcriptome in immune cells. T cell proliferation in the lymph nodes accelerates during sleep when sympathetic activity is low and lower cortisol levels allow more inflammatory-cell activity. There is also an increase in phagocytosis during the resting period. Cortisol inhibits the migration of T cells from the lymph nodes, and thus T cell migration is more active during the sleep phase.

GH and prolactin, released during SWS, enhance immune cell proliferation and the production of cytokines including IL-12 and interferon-gamma (INF-γ). IL-12 released by APC is critical to the activation of T helper cells and their differentiation in to Th1 cells. Without sufficient SWS and the release of GH and prolactin to promote IL-12, the body's ability to defend itself from viruses, intracellular bacterial disease, and cancer becomes severely impaired.

Nocturnal sleep, and SWS in the early part of the night in particular, appears to be central to IL-12 production and its induction of Th1, while later sleep supports Th2 dominance. Later in the wee hours of the day, sleep, and particularly non-SWS, also appears to promote the activity of Treg cells (natural regulatory T cells) that prevent excessive immune response such as occurs in autoimmune disease.

The activity of the immune system very much mimics the brain. During the active period (the day for humans) natural killer cells and cytotoxic T lymphocytes are active, seeking out and destroying virus cells and other aberrant cells. At night, during SWS there is encoding of immune memory as the APC transfer processed antigens to naïve T helper cells dependent on IL-12. During the latter part of the sleep cycle, in association with REM sleep, there are increased levels of serum IL-7, supporting the proliferation and differentiation of memory T cells,[i] which allows a rapid response to the antigens in the future if there is a repeat infection.

The recall and response to the repeat infection from immune memory cells will be primarily a daytime activity.[ii]

In a clinical trial where Hepatitis virus A (HVA) vaccine was given, half the subject were not allowed to sleep for the one night after its administration. Four weeks later, those who went sleepless that single night had anti-HVA antibody titers half as high as did those who slept that night.[iii] Another study divided a sample of healthy young men that had not had the flu vaccine for at least three years into two groups. Each subject was tested, and the groups had very similar anti-influenza antibody titers. About half of the men were given the flu vaccine after four nights in which they were restricted to four hours sleep. They were then further restricted to two more nights of four hours of sleep, and then given 12 hours for sleep each night for seven nights to catch up on the lost sleep and then returned to their normal sleep times. The other group of men acted as controls, sleeping their usual sleep time and also receiving the flu vaccine. Ten days after vaccination, the anti-influenza antibody titers of the sleep deprived men were 43% of that of the men who slept their normal sleep times.[iv] They had developed less than half of the immune protection from the vaccine as those who had normal sleep.

In another study, one for which I would not have volunteered, over 150 healthy men and women had their sleep times and quality assessed daily for 14 days, and then had nasal examination followed by lavage. None of the volunteers had signs or symptoms of a cold, and no viral pathogens were found in the nasal washing of the volunteers. Now comes the good part. The volunteers then had rhinovirus (RV39) drops instilled into their nose and were quarantined in separate rooms for five days. During this time they were assessed for signs and symptoms and samples were collected for viral culture. At 28 days, blood was drawn for viral antibody testing. Demographic, lifestyle, and anthropomorphic data were also collected.

The patient's data was then scored, grouping pre-exposure average sleep duration into tertiles; those sleeping <7 hours, 7 – 8 hours, and > 8 hours. They are also scored on sleep efficiency of their sleep span (percent of time asleep between lying down and waking before getting up in the morning). Sleep efficiency was scored low (<92%), middle (92 – 98%), and high (>98%) efficiency by the percent of time asleep. Compared to those getting more than 8 hours of sleep, those sleeping 7 to 8 hours each night were 63 percent more likely to develop a cold after viral exposure. Those getting less than 7 hours were almost three times (OR= 2.94) as likely to become infected. Poor sleep efficiency was an even better predictor of infection risk. Compared to those with high sleep efficiency, those who slept 92 to 98% of their sleep span were nearly four times more likely to become infected (OR= 3.94) and those with poor sleep efficiency were 5.5 times more likely to become infected.[v] No other demographic or lifestyle factor was found to be significant.

My take on this is that sleep efficiency is more important than sleep duration. This data suggests that disrupted sleep, as may be caused by OSA, (obstructive sleep apnea) especially early in the night, and thus disrupting SWS, and therefore the release of GH and prolactin required for Th1 mediated cytotoxic activity, can disrupt the ability to develop adequate immune response. Since SWS is the deepest sleep, and takes longer to fall into, it is the type of sleep most susceptible to being fractured. Fractured sleep later in the night impairs other aspects of immune function and regulation, including possibly promoting autoimmune activity.

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[i] Sleep enhances serum interleukin-7 concentrations in humans. Benedict C, Dimitrov S, Marshall L, Born J. Brain Behav Immun. 2007 Nov;21(8):1058-62. PMID:17524612

[ii] Sleep and immune function. Besedovsky L, Lange T, Born J. Pflugers Arch. 2012 Jan;463(1):121-37. doi: 10.1007/s00424-011-1044-0. PMID:22071480

[iii] Sleep enhances the human antibody response to hepatitis A vaccination. Lange T, Perras B, Fehm HL, Born J. Psychosom Med. 2003 Sep-Oct;65(5):831-5. PMID:14508028

[iv] Effect of sleep deprivation on response to immunization. Spiegel K, Sheridan JF, Van Cauter E. JAMA. 2002 Sep 25;288(12):1471-2. PMID:12243633

[v] Sleep habits and susceptibility to the common cold. Cohen S, Doyle WJ, Alper CM, Janicki-Deverts D, Turner RB. Arch Intern Med. 2009 Jan 12;169(1):62-7. doi: 10.1001/archinternmed.2008.505. PMID:19139325