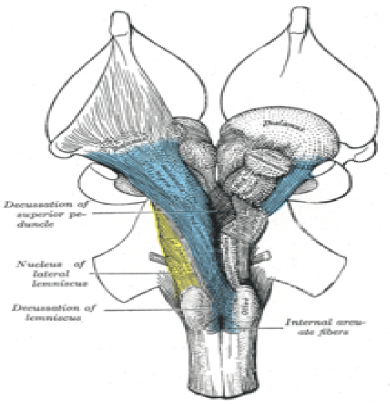

Wake up: The ‘Ascending reticular activating system’ (ARAS) and its role in consciousness & attention

Description

The reticular formation is essential for governing some of the basic functions of higher organisms and is one of the phylogenetically oldest portions of the brain.

The ascending reticular activating system (ARAS), also known as the extrathalamic control modulatory system or simply the reticular activating system (RAS), is a set of connected nuclei in the brains of vertebrates that is responsible for regulating wakefulness and sleep-wake transitions. The ARAS is a part of the reticular formation and is mostly composed of various nuclei in the thalamus and a number of dopaminergic, noradrenergic, serotonergic, histaminergic, cholinergic, and glutamatergic brain nuclei.

The ascending reticular activating system is an important enabling factor for the state of consciousness. The ARAS also helps mediate transitions from relaxed wakefulness to periods of high attention. There is increased regional blood flow (presumably indicating an increased measure of neuronal activity) in the midbrain reticular formation (MRF) and thalamic intralaminar nuclei during tasks requiring increased alertness and attention.

The reticular formation is divided into three columns: raphe nuclei (median), gigantocellular reticular nuclei (medial zone), and parvocellular reticular nuclei (lateral zone). The raphe nuclei are the place of synthesis of the neurotransmitter serotonin, which plays an important role in mood regulation. The gigantocellular nuclei are involved in motor coordination. The parvocellular nuclei regulate exhalation.

Further References

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, 19(1), 67–84.

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“Extensive studies have ascribed a role to the brainstem cholinergic system in the generation of rapid eye movement (rem) sleep and ponto-geniculo-occipital (pgo) waves. much of this work stems from systemic and central cholinergic drug administration studies. the brainstem cholinergic system is also implicated in cortical activation via basal forebrain, thalamic, and hypothalamic relay neurons. this cholinergic ascending reticular activating hypothesis has also been suggested by in vivo experiments under anesthetics and by in vitro studies using cholinergic agonists in thalamic and hypothalamic slices. during the last ten years, brainstem cholinergic neurons have been discovered to be in the peribrachial area (pbl). with the discovery of pbl cholinergic neurons, many studies were devoted to the examination of pbl neuronal activity and their connectivity. this article reviews pbl neuronal activity in behaving animals and the anatomical features of these neurons in relation to behavioral state control. the role of the pbl in the generation of rem sleep, pgo waves, and the ascending reticular activating system (aras) has been evaluated at the cellular and neurochemical level. based on recent literature, tentative mechanisms of rem sleep generation, pgo waves generation, and the cortical activation process are also outlined. © 1995.”
Edlow, B. L., Takahashi, E., Wu, O., Benner, T., Dai, G., Bu, L., … Folkerth, R. D.. (2012). Neuroanatomic connectivity of the human ascending arousal system critical to consciousness and its disorders. Journal of Neuropathology and Experimental Neurology, 71(6), 531–546.

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“The ascending reticular activating system (aras) mediates arousal, an essential component of human consciousness. lesions of the aras cause coma, the most severe disorder of consciousness. because of current methodological limitations, including of postmortem tissue analysis, the neuroanatomic connectivity of the human aras is poorly understood. we applied the advanced imaging technique of high angular resolution diffusion imaging (hardi) to elucidate the structural connectivity of the aras in 3 adult human brains, 2 of which were imaged postmortem. high angular resolution diffusion imaging tractography identified the aras connectivity previously described in animals and also revealed novel human pathways connecting the brainstem to the thalamus, the hypothalamus, and the basal forebrain. each pathway contained different distributions of fiber tracts from known neurotransmitter-specific aras nuclei in the brainstem. the histologically guided tractography findings reported here provide initial evidence for human-specific pathways of the aras. the unique composition of neurotransmitter-specific fiber tracts within each aras pathway suggests structural specializations that subserve the different functional characteristics of human arousal. this aras connectivity analysis provides proof of principle that hardi tractography may affect the study of human consciousness and its disorders, including in neuropathologic studies of patients dying in coma and the persistent vegetative

state.”
Englot, D. J., D’Haese, P. F., Konrad, P. E., Jacobs, M. L., Gore, J. C., Abou-Khalil, B. W., & Morgan, V. L.. (2017). Functional connectivity disturbances of the ascending reticular activating system in temporal lobe epilepsy. Journal of Neurology, Neurosurgery and Psychiatry, 88(11), 925–932.

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“OBJECTIVE seizures in temporal lobe epilepsy (tle) disturb brain networks and lead to connectivity disturbances. we previously hypothesised that recurrent seizures in tle may lead to abnormal connections involving subcortical activating structures including the ascending reticular activating system (aras), contributing to neocortical dysfunction and neurocognitive impairments. however, no studies of aras connectivity have been previously reported in patients with epilepsy. methods we used resting-state functional mri recordings in 27 patients with tle (67% right sided) and 27 matched controls to examine functional connectivity (partial correlation) between eight brainstem aras structures and 105 cortical/subcortical regions. aras nuclei included: cuneiform/subcuneiform, dorsal raphe, locus coeruleus, median raphe, parabrachial complex, pontine oralis, pedunculopontine and ventral tegmental area. connectivity patterns were related to disease and neuropsychological parameters. results in control subjects, regions showing highest connectivity to aras structures included limbic structures, thalamus and certain neocortical areas, which is consistent with prior studies of aras projections. overall, aras connectivity was significantly lower in patients with tle than controls ($p<0.05$, paired t-test), particularly to neocortical regions including insular, lateral frontal, posterior temporal and opercular cortex. diminished aras connectivity to these regions was related to increased frequency of consciousness-impairing seizures ($p<0.01$, pearson’s correlation) and was associated with impairments in verbal iq, attention, executive function, language and visuospatial memory on neuropsychological evaluation ($p<0.05$, spearman’s rho or kendell’s tau-b). conclusions recurrent seizures in tle are associated with disturbances in aras connectivity, which are part of the widespread network dysfunction that may be related to neurocognitive problems in this devastating disorder.”
Jones, B. E.. (2011). Neurobiology of waking and sleeping. Handbook of Clinical Neurology (Vol. 98)

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“This chapter discusses the neurobiology of waking and sleeping. waking and sleeping are actively generated by neuronal systems distributed through the brainstem and forebrain with different projections, discharge patterns, neurotransmitters, and receptors. specific ascending systems stimulate cortical activation, characterized by fast, particularly gamma activity that occurs during waking and rapid eye movement (rem) sleep. in addition to glutamatergic neurons of the reticular formation and thalamus, cholinergic pontomesencephalic and basal forebrain neurons are integral components of the ascending activating system. sleeping is initiated by inhibition of the activating and arousal systems. this inhibition is effected at multiple levels through particular gabaergic neurons which become active

during sleep. neurons in the preoptic area and basal forebrain play a particularly important role in this process. some become active during slow-wave sleep (sws), promoting deactivation, and slow-wave activity in the cerebral cortex. others discharge at progressively increasing rates during sws and rem sleep, promoting behavioral quiescence, and diminishing muscle tone. through their projections and inhibitory neurotransmitter, they have the capacity to inhibit the monoaminergic neurons and orexin (orx)neurons in the brainstem and hypothalamus."
Kinomura, S., Larsson, J., Gulyás, B., & Roland, P. E.. (1996). Activation by attention of the human reticular formation and thalamic intralaminar nuclei. Science, 271(5248), 512–515.

Plain numerical DOI: 10.1126/science.271.5248.512
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"It has been known for over 45 years that electrical stimulation of the midbrain reticular formation and of the thalamic intralaminar nuclei of the brain alerts animals. however, lesions of these sectors fail to impair arousal and vigilance in some cases, making the role of the ascending activating reticular system controversial. here, a positron emission tomographic study showed activation of the midbrain reticular formation and of thalamic intralaminar nuclei when human participants went from a relaxed awake state to an attention-demanding reaction-time task. these results confirm the role of these areas of the brain and brainstem in arousal and vigilance."
Lin, J. S.. (2000). Brain structures and mechanisms involved in the control of cortical activation and wakefulness, with emphasis on the posterior hypothalamus and histaminergic neurons. Sleep Medicine Reviews

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"Wakefulness is a functional brain state that allows the performance of several 'high brain functions', such as diverse behavioural, cognitive and emotional activities. present knowledge at the whole animal or cellular level suggests that the maintenance of the cerebral cortex in this highly complex state necessitates the convergent and divergent activity of an ascending network within a large reticular zone, extending from the medulla to the forebrain and involving four major subcortical structures (the thalamus, basal forebrain, posterior hypothalamus and brainstem monoaminergic nuclei), their integral interconnections and several neurotransmitters, such as glutamate, acetylcholine, histamine and noradrenaline. in this mini-review, the importance of the thalamus, basal forebrain and brainstem monoaminergic neurons in wake control is briefly summarized, before turning our attention to the posterior hypothalamus and histaminergic neurons, which have been far less studied. classical and recent experimental data are summarized, supporting the hypothesis that (1) the posterior hypothalamus constitutes one of the brain ascending activating systems and plays an important role in waking; (2) this function is mediated, in part, by histaminergic neurons, which constitute one of the excitatory sources for cortical activation during waking; (3) the mechanisms of histaminergic arousal involve both the ascending and descending projections of histaminergic neurons and their interactions

with diverse neuronal populations, such as neurons in the pre-optic area and cholinergic neurons; and (4) other widespread-projecting neurons in the posterior hypothalamus also contribute to the tonic cortical activation during wakefulness and/or paradoxical sleep. (c) 2000 harcourt publishers ltd."
McKinney, M.. (2005). Brain cholinergic vulnerability: Relevance to behavior and disease. Biochemical Pharmacology

Plain numerical DOI: 10.1016/j.bcp.2005.05.019
DOI URL
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"The major populations of cholinergic neurons in the brain include two 'projection' systems, located in the pontine reticular formation and in the basal forebrain. these two complexes comprise, in part, the anatomical substrates for the 'ascending reticular activating system' (aras). the pontine cholinergic system relays its rostral influences mainly through thalamic intralaminar nuclei, but it also connects to the basal forebrain and provides a minor innervation of cortex. the basal forebrain cholinergic complex (bfcc) projects directly to cortex and hippocampus, and has a minor connection with the thalamus. recent data reveal that a parallel system of basal forebrain gabaergic projection neurons innervates cortex/hippocampus in a way that seems to complement the bfcc. generally, the picture developed from more than 50 years of research is consistent with a 'global' influence of these two ascending cholinergic projections on cortical and hippocampal regions. seemingly, the bfcc acts in tandem or in parallel with the pontine cholinergic projection to activate the electro-encephalogram, increase cerebral blood flow, regulate sleep-wake cycling, and modulate cognitive function. there are quite a number and variety of human brain conditions, notably including alzheimer's disease, in which degeneration of basal forebrain cholinergic neurons has been documented. whether the corticopetal gaba system is affected by disease has not been established. studies of degeneration of the pontine projection are limited, but the available data suggest that it is relatively preserved in alzheimer's disease. hypotheses of bfcc degeneration include growth factor deprivation, intracellular calcium dysfunction, amyloid excess, inflammation, and mitochondrial abnormalities/oxidative stress. but, despite considerable research conducted over several decades, the exact mechanisms underlying brain cholinergic vulnerability in human disease remain unclear. © 2005 elsevier inc. all rights reserved."
Mesulam, M. M.. (2010). Attentional and confusional states. CONTINUUM Lifelong Learning in Neurology, 16(4), 128–139.

Plain numerical DOI: 10.1212/01.CON.0000368265.38415.35
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"The term attention refers to the preferential allocation of cognitive and neural resources to events that have become behaviorally relevant. attention is modulated by the bottom-up influence of the ascending reticular activating system and the top-down influence of association and limbic cortices. focal lesions that interfere with the bottom-up or top-down regulation of attention, or multifocal partial lesions that interrupt multiple domain-specific processing pathways, can disrupt the attentional matrix and give rise

to the acute confusional state syndrome."
Newman, J.. (1995). Thalmic Contributions to Attention and Consciousness. Consciousness and Cognition

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"A tacit assumption since the 19th century has been that the neocortex serves as the 'seat of consciousness.' an unexpected challenge to that assumption arose in 1949 with the discovery that high-frequency eeg activation associated with an alert state requires the intactness of the brainstem reticular formation. this discovery became the impetus for nearly three decades of research on what came to be known as the reticular activating system. by the 1970s, however, methodological and philosophical controversies led to general abandonment of subcortical theories of attention and consciousness, with a return to an almost exclusive focus upon the cortex. with recent advances in the neurosciences the focus is shifting once more, this time to the unique contributions of cortical, thalmic, and brainstem structures in mediating selective attention and perceptual awareness. this paper offers a nontechnical review of the history of these developments up to contemporary interest in the putative role of oscillatory eeg patterns in the integration of perceptual features of experience. it puts forward the thesis that a key to understanding attention and consciousness is an appreciation of contributions of the thalmus to these cognitive processes. © 1995 academic press. all rights reserved."
Robbins, T. W.. (1997). Arousal systems and attentional processes. In Biological Psychology (Vol. 45, pp. 57–71)

Plain numerical DOI: 10.1016/S0301-0511(96)05222-2
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"Unitary concepts of arousal have outlived their usefulness and their psychological fractionation corresponds to a similar chemical differentiation of the reticular formation of the brain. neurobiological characteristics of the monoaminergic and cholinergic systems can be described in terms of their anatomical, electrophysiological and neurochemical properties. functional studies suggest that the coeruleo-cortical noradrenergic system, under certain circumstances, is implicated in processes of selective attention, that the mesolimbic and mesostriatal dopaminergic systems contribute to different forms of behavioural activation, and that the cortical cholinergic projections have fundamental roles in the cortical processing of signals, affecting attentional and mnemonic processes. the ascending serotoninergic systems contribute to behavioural inhibition and appear to oppose the functions of the other systems in several ways."
Siegel, J.. (2004). Brain mechanisms that control sleep and waking. Naturwissenschaften

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“This review paper presents a brief historical survey of the technological and early research that laid the groundwork for recent advances in sleep-waking research. a major advance in this field occurred shortly after the end of world war ii with the discovery of the ascending reticular activating system (aras) as the neural source in the brain stem of the waking state. subsequent research showed that the brain stem activating system produced cortical arousal via two pathways: a dorsal route through the thalamus and a ventral route through the hypothalamus and basal forebrain. the nuclei, pathways, and neurotransmitters that comprise the multiple components of these arousal systems are described. sleep is now recognized as being composed of two very different states: rapid eye movements (rems) sleep and non-rem sleep. the major findings on the neural mechanisms that control these two sleep states are presented. this review ends with a discussion of two current views on the function of sleep: to maintain the integrity of the immune system and to enhance memory consolidation. [references: 114]”
Yeo, S. S., Chang, P. H., & Jang, S. H.. (2013). The Ascending Reticular Activating System from Pontine Reticular Formation to the Thalamus in the Human Brain. Frontiers in Human Neuroscience, 7

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“Introduction: action of the ascending reticular activating system (aras) on the cerebral cortex is responsible for achievement of consciousness. in this study, we attempted to reconstruct the lower single component of the aras from the reticular formation (rf) to the thalamus in the normal human brain using diffusion tensor imaging (dti). methods: twenty six normal healthy subjects were recruited for this study. a 1.5-t scanner was used for scanning of diffusion tensor images, and the lower single component of the aras was reconstructed using fmrib software. we utilized two rois for reconstruction of the lower single component of the aras: the seed roi – the rf of the pons at the level of the trigeminal nerve entry zone, the target roi – the intralaminar nuclei of the thalamus at the level of the commissural plane. results: the reconstructed aras originated from the pontine rf, ascended through the mesencephalic tegmentum just posterior to the red nucleus, and then terminated on the intralaminar nuclei of the thalamus. no significant differences in fractional anisotropy, mean diffusivity, and tract number were observed between hemispheres ($p > 0.05$). conclusion: we reconstructed the lower single component of the aras from the rf to the thalamus in the human brain using dti. the results of this study might be of value for the diagnosis and prognosis of patients with impaired consciousness.”
Young, G. B.. (2011). Impaired Consciousness and Herniation Syndromes. Neurologic Clinics

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“This article reviews alterations in consciousness related to intracranial mass lesions. such lesions can produce impairment of consciousness by their strategic location within components of the ascending reticular activating system or secondarily by compressing or distorting this system, interfering with its synaptic and neurochemical functions. this review concentrates principally on this secondary mechanism. © 2011.”

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