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Conceptual Insight of Etiopathogenesis of ADHD in Ayurvedic Idiom

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ABSTRACT

Attention-Deficit Hyperactivity Disorder (ADHD) is a childhood psychiatric disorder found universally across countries with persistently rising incidences. Etiopathogenesis of ADHD is based on multifactorial etiological pathways concerning with neurobiological, genetic and environmental aspect. Although various causal links of the disease are precisely established in modern psychiatry, complete cure of ADHD patient without side-effect is till underachieved target for modern community. In Ayurvedic literature, ADHD is not described as separate clinical entity and hence an effort has been framed out to establish the etiopathogenesis*(samprapti)* of ADHD in Ayurvedic idiom. The conceptualization of *Sampropti*of ADHD is purely based on the concept of vitiated *dosh-dushyasammurchchana*in the active presence of *khavaigunya.* This knowledge of etiopathogenesis may reveal the specific nature of brain dysfunction in ADHD and may help to understand the development of symptomatology of the disorder and further its precise nature to respond with various treatment strategies described in Ayurveda.

Keywords: ADHD, Etiopathogenesis, *Samprapti, Khavaigunya*

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INTRODUCTION

According to DSM IV, ADHD is a childhood psychiatric disorder, defined according to the presence of symptoms in three domains: inattention, impulsivity and hyperactivity (motor over activity) [1]. These features also observed in each individual at comparable level of normal development. But when it becomes excessive it leads to impairment of academic, occupational and social settings of an individual. In other words the children with ADHD are at higher risk of academic under achievement; also some may fail to complete their formal schooling. If ignored and doesn't treat they may show more severe consequences in the form of conduct disorder, delinquency and further adult antisocial personality disorder.

AIMS & OBJECTIVES

- To validate the contribution of components of *samprapti* (i.e. *tridoshas, trigunas, khavaigunya, prakriti*etc.) in neurobiology of ADHD.
- To establish the *etiopathogenesis* of ADHD in Ayurvedic idiom to understand the development of symptomatology.

REVIEW OF CONCEPT

According to Ayurveda, the psychiatric disorders are derived from intellectual blashphemy (*pragyaparadha*) which resulted into impairment of *dhee, dhriti and smriti,* thereby vitiating the *tridoshas* and *trigunas*. [2] These factors altogether with numerous *vyadhihetu (Sahaja, Agantuja* etc.) and pre existing*"Khavaigunya*" [3] reside at the place of *Manovahastrotas*, which ultimately resulting into symptoms of disorder. Keeping *Ayurvedic* fundamentals in mind, an effort has been made to explain the *samprapti* of ADHD on the basis of brain region dependent processing of information.

1. Locus Ceoruleus:

LC is a large cluster of norepinephrine neurons in the dorsal pons which has extensive projections to almost every level of neuro-axis. It involves in selective processing of visual and auditory environmental stimuli and stimuli received from somatic and visceral inputs by evoking large phasic increase in firing. Responsiveness to sensory signals is modulated by somatodendritic alpha-2 autoreceptors. When LC released excessive NE in response to stimuli, these autoreceptors get stimulated to suppress the basal firing and to enhance evoked response in the nucleus. Peripheral epinephrine is another input which provides tonic inhibitory control to LC for further regulation.

Thus, the loss of either of these two inputs to the LC causes hyperactivity that disrupts stimulus evoked responding which might fail to select the relevant novel stimuli and thereby deficits in vigilance and sustained attention [4].

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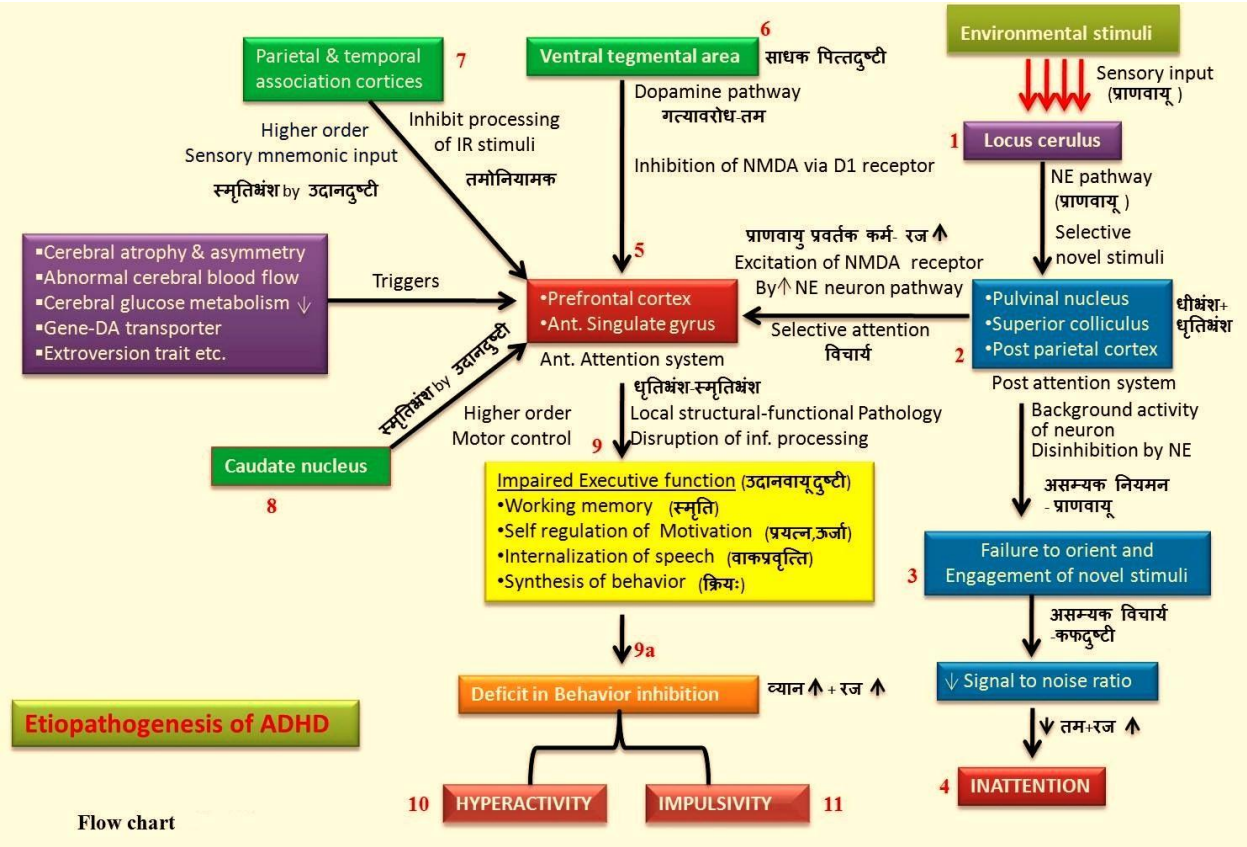
According to *Ayurveda 'pranavayu*' [5] is responsible for the transmission of sensory inputs from sense object to their target site (i.e. *manas*) where various *manovishayas* are involved in the due processing of stimuli [6]. At the level of locus coeruleus the *chintyavishay* of *manas* is worked for selection of relevant stimuli and rejection of irrelevant sensory objects. [7**] (Flow chart-step1)**



If the *chintyavishayas* are not properly carried out by *pranavayu*, the desired novel stimuli may remain either unattended or irrelevant stimuli may get selected. Here, the hyper-functioning of NE pathway acts like *rajas guna*, which is usually regulated by *'niyaman*' quality of *tamas guna* [8] and here it is denoted by somatodendritic alpha -2 autoreceptor and epinephrine inputs.

The pathophysiology of ADHD incorporates dysfunction of multiple neurotransmitter systems. The selective novel stimuli perceived by Locus ceoruleus is processed by attentional functions that are distributed into 'posterior attention system' and 'anterior attention system' of cortex.

2. Posterior attention system:

PAS includes the superior parietal cortex (SPC), the superior colliculus and pulvinar nucleus which receive dense innervation of NE neurons from the LC [9]. Norepinephrine

reduces the background activity of neurons and makes them more attentive. This primes the posterior attention system to orient to and engage in novel stimuli thereby increasing the signal to noise ratio of target cell. (SNR -means to attend every desired task related stimuli) **(Flow chart-step 3)**

Thus inability of NE to prime the posterior attention system may account for the attentional problems like inattention, sustained attention, focused attention etc. **(Flow chart-step 4)**

- The perception of stimuli at the level of LC (irrespective of novel or irrelevant) are feed forward to Posterior Attention System, where the hyper functioning of *pranavayu* and *rajas guna* fail to regulate the *manas karma* i.e. *chintya*and *vicharya* which consequently may impair *dhee&dhriti*.**(Flow chart-step 2).**
- Due to impairment of *dhee*, the capacity to distinguish between desirable and undesirable object, is hampered and this will lead to inability to select novel information and to ignore environmental distractions [10] **(Flow chart-step 3).**
- Also whatever information perceived by *dhee*, is further retained by *dhriti*. *Dhriti* is a function of *prakritkaphadosha* which is attributed by its *sthiratva* quality [11] and also a*dhriti* is a quality attributed to *rajas guna*. [12] Thus the joint effect of increased *rajas guna* and decreased *kaphadosha*, are contributed to state of inattention (*Dhriti* impairment), thereby a child may be deficit in sustaining attention, highly distractible and often loosing things. **(Flow chart-step 4)**

Back to modern aspect of pathophysiology of ADHD, the second important attentional locality is 'Anterior attention system' or otherwise known as anterior executive system, as it serves executive functions.

3. Anterior Attention system:

Attentional function then shifts to anterior executive system which consists of prefrontal cortex (PFC) and anterior cingulate gyrus (ACG).The responsiveness of PFC and ACG to the incoming signals, is modulated primarily by dopaminergic (DA) input from ventral tegmental area in the midbrain. These ascending DA fibers stimulate to postsynaptic D1 receptors on pyramidal neurons in the PFC and ACG which in turn facilitate excitatory NMDA receptor inputs from the posterior attention system. Thus, DA selectively gates excitatory inputs to the PFC cingulate gyrus thereby reducing irrelevant neuronal activity during the performance of executive function.

Therefore, the loss of dopaminergic ability to get inputs to the anterior executive system may be linked to deficits in executive function, characteristic of ADHD [13].

- The attentional shift from post attention system to anterior executive system is mediated by *pranavayu* where it leads to excitation of NMDA receptor which can be symbolized here to *rajas guna* [8]. **(Flow chart-step 5)**

- The over excitation of rajas guna is suppressed by *tamas guna* [8].This may connote with D1 receptor of dopamine system. At the level of PFC, dopamine serves the function similar to *sadhak pitta* [14] and involved in *buddhi* and *medha* oriented activities. **(Flow chart-step 6)**

4. Association areas of cortex:

Deficit in behavioral inhibition (i.e. hyperactivity and impulsivity) is another key characteristic of ADHD which evolved from NE receptor dysfunctioning mediated by association areas of cortex.

Two important areas viz. parietal and temporal association cortices provide higher order sensory and mnemonic input (memory dependent information) to PFC. These inputs facilitate cognitive processing required for executive functions [15]. **(Flow chart-step 7).**

The PFC also receives the inhibitory connections from these cortices which suppress the processing of irrelevant sensory stimuli, thereby protecting the ongoing cognitive task from interference [16].

Caudate nucleus is another regulating body which provides inhibitory connections to PFC for higher order motor control. **(Flow chart-step 8)**

These inhibitory connections of PFC are evolved from NE neuron projections from LC. These NE fibers stimulate post-synaptic alpha-2 adrenoreceptors, which inhibit spontaneous cell firing, thereby enhancing signal-to-noise ratio of PFC neurons. These receptors may facilitate to PFC to-

- Process the task related stimuli
- Suppress the task irrelevant stimuli and
- Inhibit behavior

Therefore, diminished brainstem NE activity and release, cause a partial denervation of post synaptic alpha-2 receptors in the PFC which disrupts the inhibitory control functions of the PFC. In turn, this produces the deficits in behavioral inhibition [4**] (Flow chart-step9,9a).** This inhibitory deficit causes ancillary impairment in four executive functions that require inhibition for their effective performances viz.-

i. Working memory
ii. Self regulation of affect / motivation and arousal
iii. Internalization of speech (e.g. rule governed behavior, reflection)
iv. Reconstitution (e.g. synthesis of behavior, verbal fluency)

The impairment in these functions, yield many cognitive and behavioral deficits associated with ADHD. Since these four cognitive functions serve to regulate motor functions via internal representations and self-directed actions, hence impairments in these abilities contribute to the impulsivity & Hyperactivity. **(Flow chart-step 10, 11).**

The primary information processing is carried out at the level of *Manas* with the aid of its *Manovishayas* [16]and *manokarmas* [17] later on; it transfers to *buddhi* for complex processing. The functional units of *buddhi*, especially, *dhriti* and *smriti*plays a crucial role to integrate the sensory and memory information which is essentially required for higher order cognition. This process is depicted by following way –

- ***Dhriti***– In higher order cognition, *dhriti* is subscribed to retain or stabilize the sensory information for its further representation and also to control the *manas* to devoid from indulging in harmful and undesirable objects. [18] Since the signals of NE pathway (Via parietal & temporal association cortices) suppresses the undesirable ongoing task of neuron and provide some sensory inputs to PFC, hence it may exemplify with the functions of *dhriti*. Hence, the degradation of *dhriti*, as a result, makes person unable to complete the task uninterruptedly or to stay at one task until it finish, thereby resulting into deficient cognition and disorganized behavior.
- ***Smriti***– Retrieval of past experiences is termed as *smriti.* By means of NE fibers, association cortices provide higher order sensory-mnemonic inputs to PFC which utilizes the previously learned experience (*Smriti*) in reference to current ongoing task to achieve higher order executive functions. In addition, the caudate nucleus provides higher order motor mnemonic inputs to PFC which utilize to inhibit the irrelevant voluntary movement irrespective to current task.
  Thus, the degradation of *smriti*alters the ability of child to recall the past experiences and consequently show deficient behavior inhibition and poor cognition.
- At *doshik* level, the factor causing '*Dhritibhransha*' is a 'deranged *kapha*' and 'increased *raja*', while 'deranged *udanvayu*' is the factor cause for '*smriti bhransha*' [19].
- Also, the factor exclusively responsible for higher order executive function is *udan vayu* [19] which can be illustrated as follows-

  i. Working memory – by *smriti*
  ii. Self regulation of affect/ motivation/ arousal – by *prayatna, urja*
  iii. Internalization of speech – by *vakpravritti*
  iv. Synthesis of behavior – by *kriya* etc.
- On a similar note, the *vyanvayu i*s exclusive *doshik* factor, which is responsible for voluntary movement, hence the derangement of *vyanvayu* causes poor response inhibition (i.e. impulsivity) and disorganized behavior [20] (i.e. hyperactivity)

Thus, *dhritibhransha* and *smritibhransha* jointly account for impaired executive function and deficit behavior inhibition, i.e. impulsivity altogether manifest clinical presentation of ADHD.

There are some ADHD triggers, which influence the disease at various levels viz. symptoms, severity, prognosis and treatment response these are as follows-

- ✓ Non-specific structural abnormalities e.g. cerebral atrophy and asymmetry [21].

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- ✓ Altered cerebral blood flow e.g. hypo-perfusion at striatal area and hyper-perfusion at post cortical regions [22].
- ✓ Altered cerebral glucose metabolism e.g. reduction in areas like premotor and superior PFC, also striatum, thalamus, hippocampus, cingulate gyrus etc [23].
- ✓ Altered catecholaminergic neurotransmission especially increased levels of dopamine and norepinephrine [24].
- ✓ Some genetic alterations, e.g. polymorphism in dopamine (DA) transporter gene and DAD2 and DAD4 receptor gene [25].

In *Ayurvedic* idiom, the above mentioned triggers may often termed as "*Khavaigunya*" [3] which when accompanying with *vatajaprakriti*[26] influence the disease multidimensionally.

Probable etiopathological markers of ADHD as per Modern in relation to Ayurveda			
	Modern	**Ayurveda**	**Ref.no.**
1.	**Sensory nerves**	**Pranavayu**	**5**
2.	**NE Pathway**	**Functions of Manas affected by Rajas guna**	
3.	**Somatodendritic α-2 auto receptor & epinephrine inputs**	**Tamasguna**	**8**
4.	**Signal to noise ratio**	**Chintya-Vicharyadi functions of Manas (regulated by Pranavayu& Rajas guna)**	**7**
5.	**Attention**	**Dhriti–Kaphadosha**	**11**
6.	**Inattention**	**Rajas guna**	**12**
7.	**Impairment in attention**	**Dheebhramsha&Dhritibhramsha (Kapha + Rajas)**	**11,12**
8.	**Functions of Dopamine**	**Functions of Sadhak Pitta**	**14**
9.	**Higher order sensory, mneumonic inputs & Higher order motor control**	**Functions of Udanavayu**	**19**
10.	**Behavioral inhibition**	**Dhritibhramsha&Smritibhramsha (Kaphadosha + Udanavayu)**	**11,19**
11.	**Impulsivity & Hyperactivity**	**Impaired Vyanavayu**	**20**
12.	**ADHD triggers**	**Sahaj, AgantujVyadhihetu leading to Khavaigunya**	**3**
13.	**Extraversion trait**	**VatajPrakriti**	**26**

CONCLUSION

- In *Ayurvedic* idiom, *samprapti*of ADHD is evolved from intelectualblashphemy in active presence of *khavaigunya* and *Vatajaprakriti* which may result into alteration of *tridoshas*&*trigunas*.
- For genesis of inattention, decrease in *kaphadosha* and increase in *rajas guna* may particularly be responsible.
- Moreover, impairment in higher-order cognition may arise as a result of alteration of functions of *manas*&*buddhi.* As *sadhakpitta* may cause for *dhritibhransha* and alteration in *chintya-vicharyadi* functions of *manas*while *udanvayu* may causefor*dhritibhransha*.
- Also, the deficits in behavior inhibition may generate from vitiated *vyanvayu*which is executed by Hyperactivity & Impulsivity.

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