DEFAULT MODE NETWORK ALTERATIONS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER AND METHYLPHENIDATE EFFECTS

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ABSTRACT
Since 2001 when default mode network (DMN) was first proposed, it became one of the most demanding research themes in neurological and psychiatric disorders. Therefore DMN alterations were discovered in attention-deficit/hyperactivity disorder (ADHD) among other mental diseases. DMN or task-negative(TN) mode represents a resting state of brain function inversely correlated with task-positive(TP) mode or attention network, thus it is observed to be deactivated in various goal-oriented tasks. Methylphenidate is a widely-used medication in ADHD and its effect on DMN may complete the mechanisms by which it can ameliorate the attentional difficulties. These findings help to better understand the neurocognitive models of mental disorders in order to provide new treatments that may be more effective.

Keywords: attention-deficit/hyperactivity disorder, default mode network, methylphenidate.

INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is characterized by difficulties in concentration leading to unfinished tasks and low perseverance, hyperkinetic behavior which disrupts activities that demand sitting, as in school or waiting in a queue and impulsiveness causing disregard for the rules to a certain extent. These symptoms may be frequently accompanied by impaired cognitive functions, but symptoms like dissocial behavior can also be present, thus in the follow-up a conduct disorder should be under observation. The disorder usually manifests in the first 5 years, but there is a peak of diagnosis at 7 years old concurrently with school integration [1].

Default mode network (DMN), first introduced in 2001, describes the resting state of brain function, the equilibrium state of the brain or the baseline level of neuronal activity. DMN was studied by neuroimaging techniques: positron emission tomography(PET) and functional magnetic resonance imaging(fMRI), but in some studies electroencephalography(EEG) was also used. The DMN or the task-negative(TN) system is anti-correlated with the task-positive(TP) mode, attention network or cognitive control network(CCN) which consists of ventral attention network(VAN) and dorsal attention network(DAN). DMN was found to comprise brain regions such as the posterior cingulate, adjacent precuneus and ventral medial prefrontal cortex(vmPFC) which exhibit an attenuated activity while focused attention [2,3,4].

Other brain areas that have been associated with DMN are dorsal medial prefrontal cortex(dmPFC) and lateral

parietal cortex and they also present decreased activation during the time of task performance. The vmPFC has an important role in regulation of emotion(social behavior, mood control), attention and motivational drive, the dmPFC exemplifies self-referential mental activity and the posterior components of DMN(posterior cingulate, precuneus, lateral parietal) are involved in remembrance of previous experiences [5].

MATERIALS AND METHODS

The electronic database PubMed was searched for the most representative articles on ADHD and DMN alterations that occur in the development of this disease. The effects of methylphenidate on these DMN modifications were also studied. The number of scientific studies show an increased interest in DMN and its significance in mental illness.

RESULTS

To fully comprehend the role of the DMN in ADHD and in the other mental disorders, it is fundamental to mention that TN network processes stimulus-independent thoughts thus the more activated, the lower performance during a task [3]. Also there are significant differences between adult DMN and children DMN, the latter is more segregated and becomes more integrated as it approaches its final configuration. Further research was exigent since the results of early studies were inconsistent, behavioral alterations in ADHD being bound to either a hyper or a hypoconnectivity of the rest state network. This inconsistency may exhibit variations in methodology. In addition, the complexity of activation between nodes of TN system and their interaction with components of TP network have raised a new wave of research [6].

One of the first findings states an unclear and undefined dysfunction of DMN and a variable response to attention in ADHD [7]. Later discoveries sustain the hypothesis that the decreased suppression of TN network may be involved in ADHD neural pathways. Therefore during task performance it is shown that the DMN presents increased activity [8].

Modified connectivity between VAN and DMN is observed in children with ADHD, thus the anti-correlations between TP network and TN mode are reduced or absent in the mentioned disorder. Moreover, the degree of these modifications illustrates symptom severity. Additional observations account for hypoconnectivity within TN network compared with the results of other studies that revealed a time delay in the maturation of DMN scarcely connected by the age of 9 years old and which becomes more integrated through childhood and adolescence until young adulthood. Possible disconnection within cingulum bundle may interrupt the neural transmission between posterior and anterior DMN. Furthermore, significant right lateralization of abnormal rest state connections is detected [9, 10, 11].

Recent studies also suggest that alterations of the DMN in ADHD comprise a sustained activation which is thought to result in impaired task ability. Suppression of the DMN by the CCN is proven to be less significant compared to the control group [12,13].Some results emphasize the activation of precuneus area during cognitive challenge [14]. Interestingly, a higher negative connectivity between TN and TP networks is observed in female subjects and in addition, a greater connectivity within the rest state mode may explain the 2:1 ratio between male and female in ADHD, the mentioned data demands validation from further studies, particularly because this was a clinical observation without a plausible explanation so far [15].

Methylphenidate is a widely-used medicine in ADHD, its effects on the DMN are proven to regulate the connectivity within TN network and the inverse synchronization

with TP system [16, 17]. Up to date, most studies sustain these findings, except one study that found no significant effect of methylphenidate on DMN. Normalized deactivation of rest state by methylphenidate during sustained attention is detected to occur in medial PFC, precuneus and posterior cingulate cortex [18].

CONCLUSIONS

All these findings regarding DMN alterations suggest a central theme in the pathology of ADHD and even more surprisingly, DMN has certain roles which are only partially discovered until present days. Further research is needed to correlate current available medication for treating ADHD with effects on the discussed baseline level of brain and possibly to develop new chemical formulas which may be more effective. Overall, neuroimaging techniques have opened doors that seemed impossible to open only 20 years ago and they helped us understand our brain and we still search for answers.

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