Title: Abnormal Structure and Function of Parietal Lobe in Individuals with Attention Deficit-Hyperactivity Disorder (ADHD): A Systematic Review Study

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Abstract

Introduction: Abnormal brain structure and function has been described in individuals with Attention deficit hyperactivity disorder (ADHD). This study aimed to investigate the alteration of the parietal lobe structure and function in individuals with ADHD.

Methods: In this systematic review, we searched English papers in accordance with the PRISMA approach. Studies were published between January 2010 and May 2021. Our search was conducted in two parts. Our first search was in July 2020, and our final search ended in June 2021. A literature search identified 20 empirical experiments.

Results: In general, functional magnetic resonance imaging (MRI) studies described low activity and poor connectivity, structural MRI study has reported less gray matter of this lobe, and an echo study described atrophy, electroencephalographic studies reported less connectivity of the parietal lobes in ADHD. Furthermore, the transcranial direct current stimulation intervention has shown activation of this lobe improves attention and executive functions in children with ADHD, and finally Deep Transcranial Magnetic Stimulation study has shown activation of this lobe improves working memory.

Conclusion: Functional and structural alteration of the parietal cortex has been described in ADHD, which have a causal relationship with cognitive impairments. In sum, all included studies described abnormal structure, function, or connectivity of the parietal lobe or improvement of cognitive functions with stimulation of the parietal lobe.

Keywords: Attention deficit disorder with hyperactivity (ADHD); Parietal lobe; Executive functions; Systematic review

Introduction

Attention deficit hyperactivity disorder (ADHD) as a neurodevelopmental disorder is characterized by two main symptoms: hyperactivity-impulsivity and attention deficit (American Psychiatric Association, 2013). One well-documented theory to explain the behavioral symptoms in children with ADHD is dysexecutive function theory (Barkley, 2020). Individuals with ADHD experience a variety of dysexecutive functions such as inability to start, focus, persist, and shifting attention, keep constant effort and alertness, cope and regulate emotions, remember to-be-learnt material, and finally regulate their actions (Brown, 2009; Rodríguez et al., 2021; Staff et al., 2021).

Executive functions (EFs) as an umbrella term cover several domains such as working memory, cognitive flexibility, and inhibitory control (Burgess & Simons, 2005; Espy, 2004; Lehto, Juujärvi, Kooistra, & Pulkkinen, 2003; Miller & Cohen, 2001). Impaired EFs is a non-specific syndrome, which has been identified in numerous psychiatric disorders, including autism spectrum disorder (Shiri, Hosseini, Pishyareh, Nejati, & Biglarian, 2015), addiction (Baler & Volkow, 2006), conduct disorder (Fairchild et al., 2009), depression (Ajilchi & Nejati, 2017; Tavares et al., 2007), obsessive-compulsive disorder (Penades et al., 2007), and schizophrenia (Barch, 2005). Furthermore, some non-executive functions are impaired in individuals with ADHD such as emotional processing (Borhani & Nejati, 2018), reward processing (Nejati, Sarraj Khorrami, & Nitsche, 2020) and spatial processing (Jung, Woo, Kang, Choi, & Kim, 2014; Soluki, Nejati, & Fathabadi, 2020). Furthermore, in the study of the neural correlates of ADHD, the majority of neuroimaging studies stressed on the prefrontal cortex as the area of interest (Hesslinger et al., 2002; Pironti et al., 2014; Samea et al., 2019; Schulz et al., 2017; Seidman et al., 2006; Wolf et al., 2009; Wu et al., 2020)

Beyond the prefrontal cortex and EFs, the parietal cortex, and the respective perceptual functions, plays a crucial role in psychopathology of ADHD (Dunn & Kronenberger, 2013; Schulz et al., 2017; Silk, Vance, Rinehart, Bradshaw, & Cunnington, 2008; Vance et al., 2007). Individuals with ADHD experience some impairments in spatial perception, spatial working memory, visual recognition, and spatial reaction time (Banaschewski et al., 2006; Rhodes, Coghill, & Matthews, 2004, 2005). Given the

Posner's attentional network, individuals with ADHD are impaired in all attentional networks including alerting (Oberlin, Alford, & Marrocco, 2005), executive (Oberlin et al., 2005) and orienting (Collings & Kwasman, 2006). Sensory processing and integration problems, as another function of parietal cortex, are impaired in individuals with ADHD (Ghanizadeh, 2011; Mulligan, 1996) and abnormal perceptual function leads to hyper or hypo sensitivity to some modalities in individuals with ADHD With respect to the deficient perceptual functions in individuals with ADHD, which fundamentally involves the parietal lobes (Kamath et al., 2020), we aimed to review abnormal structure and function of the parietal lobes in individuals with ADHD.

Materials & Methods

The present study was performed by the guidelines of systematic review studies of PRISMA (Moher, Liberati, Tetzlaff, Altman, & Group, 2009).

Search strategy: The required information was provided by reviewing scientific databases including Web of Science, Science Direct, Springer, PubMed, and Google Scholar. Studies published in English between January 2010 and May 2021 were reviewed. We searched for resources once in July 2020 and again in June 2021.

Keywords: We searched the following keywords: attention deficit disorder (ADD), hyperactivity, attention deficit-hyperactivity disorder (ADHD), parietal (lobe), posterior parietal cortex (PPC), inferior parietal lobe (IPL), superior parietal lobe (SPL), angular gyrus (AG), supra marginal gyrus (SMG).

Inclusion & exclusion criteria: Articles that were available in full text in English at the desired period were entered in the present review.

Data extraction: For checking the relevance of the searched articles with the structure of the present study, first the titles, then the abstracts, and finally the whole text were independently were checked by the authors, then the authors agreed which article would remain or which would be deleted. A total of 79 articles was selected, and finally, 20 articles remained (see Fig.1). After extracting the required information, the results were first summarized in the data table (see table 1 and 2) and then analyzed.

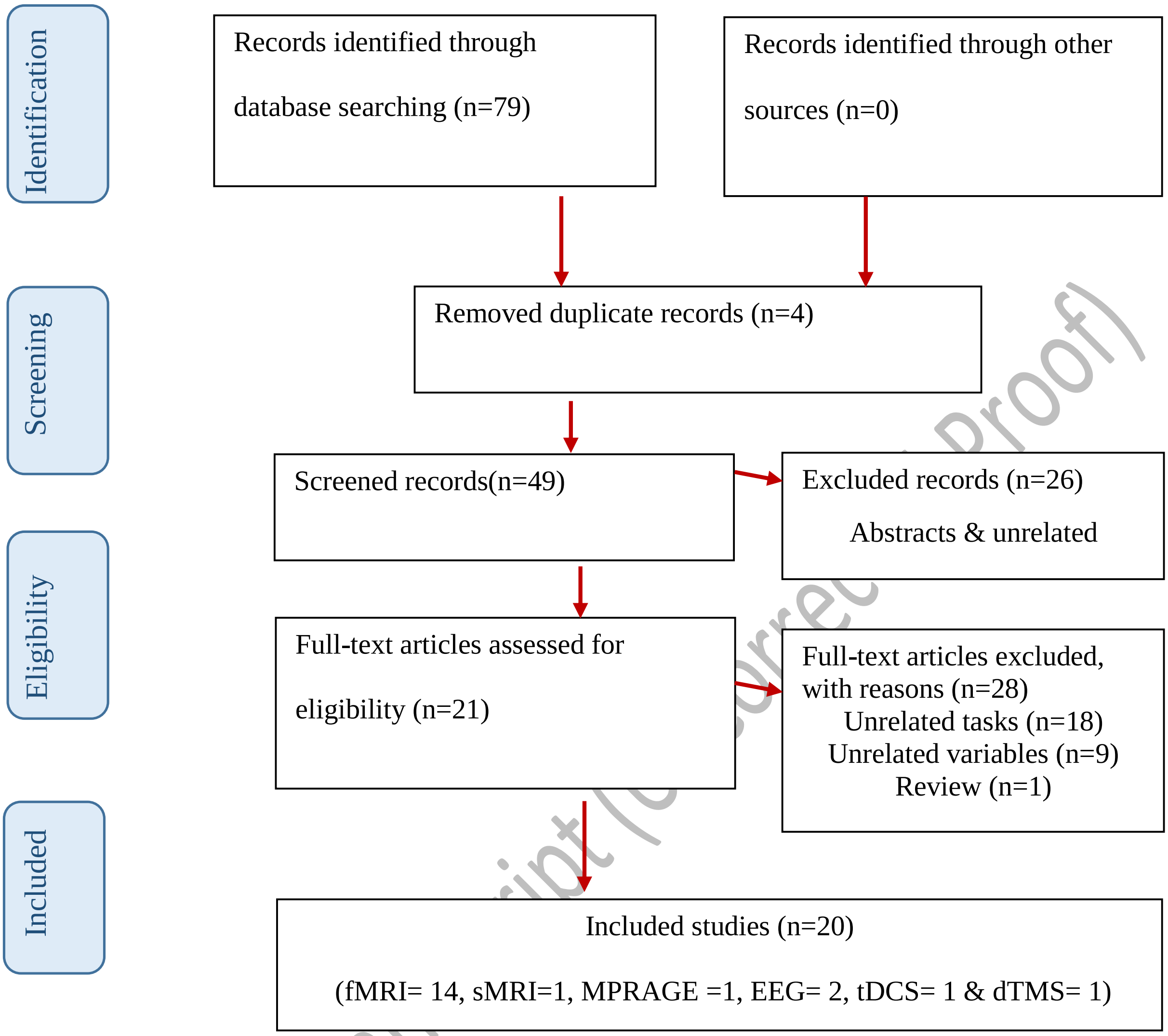

Fig. 1. Flow diagram of literature search and study selection. Note: fMRI: functional magnetic resonance imaging, sMRI: structural magnetic resonance imaging, MPRAGE: magnetization prepared rapid gradient recalled echo, EEG: electroencephalograms, tDCS: transcranial direct current stimulation, dTMS: Deep Transcranial Magnetic Stimulation.

Results

Twenty studies were included in the review, which examined 1207 participants in total, 746 participants with ADHD, 461 healthy control. Mean participant age range was 4.92 to 40.26 years old. Notably, the wide age range of participants could be explained by the diagnosis of

ADHD from childhood to adulthood. Sample sizes ranged from 17 to 188. In what follows, we summarized the results of the included studies based on methods.

Functional magnetic resonance imaging (fMRI) studies. In individuals with ADHD, desynchronization of the PPC, the precuneus and the SPL, has been described during irrelevant speech or music in the background of a film (Salmi et al., 2020). Resting-state fMRI has indicated lower degree of centrality in the default mode network (DMN) in children with ADHD (Jiang et al., 2019). This study indicated a decentralized organization (line-like topology) in the frontal-parietal attention network in children with ADHD in contrast to the more centralized organization (star-like topology) in typically developing (TD) children. Another fMRI study found drug naïve individuals with ADHD show more activation of the bilateral inferior parietal lobe during inhibition, measured by stop-signal task, and less activation in the left parietal cortex during shifting attention, measured by switch task (Berberat et al., 2021). Kolodney et al (2020) found during an inhibitory control task (go/ no-go), in individuals with ADHD with lower symptoms, the cooperation of the intraparietal sulcus (IPS) and the right inferior frontal gyrus (IFG) is increased. Whereas, in individuals with ADHD with severe symptoms no alteration in the activity of the parietal cortex is observed (Kolodny et al., 2020).

Also when adults with the previous ADHD express facial emotion (included happy and fearful expressions), the activity of the left IPL increased during fearful facial expression. Besides, during visual exposure to happy faces higher functional connectivity is visible among the posterior cingulate cortex, right ventral frontal cortex, right dorsal parietal cortex (DPC) and left temporoparietal junction (TPJ) in the individuals with former ADHD (Lindholm et al., 2019).

Bachman et al (2018) found increased brain activation on the bilateral IPL, the right posterior insula, and the right precuneus in individuals with ADHD during performing N-back task, which was associated with lower scores reported in inattention and memory problems (Bachmann et al., 2018). Schulz et al. (2017) described lower activation of the right orbitofrontal cortex, the inferior frontal cortex, and parietal lobe in individuals with ADHD during stimulus and response conflict task (Schulz et al., 2017). Another resting-state fMRI study found children with ADHD, compared with TD peers, showed weaker connectivity between the right anterior prefrontal cortex (PFC) and the right ventrolateral PFC and between the left anterior PFC and the right IPL during continuous performance and spatial span tests. This findings was associated with symptoms of impulsivity, opposition-defiance, impaired response inhibition and attentional control (Lin, Tseng, Lai, Matsuo, & Gau, 2015). Treatment by atomoxetine (ATMX) was associated with increased fMRI activation of the parietal cortex, the dlPFC, and the cerebellum during completing a multi-source interference task (MSIT) in individuals with ADHD (Bush et al., 2013). As well as fMRI with a rapid event-related design in adult ADHD showed less activation in the frontal, the supplementary, and the parietal eye fields during the antisaccade task when preparing to execute an antisaccade (Schwerdtfeger et al., 2013). Furthermore, using fMRI during phonological and visual–spatial n-back tasks have shown activation of the fronto-parietal network for working memory tasks in adults with and without ADHD. Also exhibited the intensity of the activation was greater in individuals with ADHD. The control group has exhibited increased brain activation over the fronto–parietal network in response to increased phonological working memory load. However, individuals with ADHD have shown a greater decrease in brain activation over the left fronto-parietal network (Ko et al., 2013). Also drug-naïve ADHD children showed decreased activation of the IPL and bilateral occipital, caudate nucleus, cerebellum, and functionally connected brainstem nuclei (Massat et al., 2012). The reduced activity also has been observed during CPT in the caudate nuclei, the anterior cingulate cortex, and the parietal cortical structures, the right IPL and the left SPL, in individuals with ADHD. Less activation of the left SPL was associated with impulsivity and hyperactivity and both right IPL & left SPL has a relationship with inattention symptoms in individuals with ADHD (Schneider et al., 2010). In general, fMRI studies described an alteration in the structure and function of the parietal lobe in individuals with ADHD, which indicates lower performance of the parietal lobe in this group.

Structural magnetic resonance imaging (sMRI) study. A sMRI study described a lower global and local grey matter volumes within clusters in the bilateral frontal, right parietal, and right temporal regions in individuals with ADHD compared to TD (Vilgis, Sun, Chen, Silk, & Vance, 2016).

Magnetization prepared rapid gradient recalled echo (MPRAGE) image study. An MPRAGE study described a reductions of cortical volume in the frontal, parietal, and temporal cortices are visible in young children with ADHD (Jacobson et al., 2018).

Electroencephalogram (EEG) study. Individuals with ADHD have manifested significantly less parietal theta rhythm and event-related (de) synchronisation (ERS) during inhibition and response trials, during visual continuous performance test. As well as they had an increase in parietal alpha rhythm and ERS during inhibition and action. Furthermore, lower fronto-parietal connectivity has been described in individuals with ADHD (Cowley, Juurmaa, & Palomaki, 2020). Another ERP study described less connectivity among temporal, frontal, and parietal cortices during an oddball task in individuals with ADHD (Chen et al., 2021).

Transcranial direct current stimulation (tDCS) study. Anodal tDCS over the right PPC impoved attentional functioning in attention networks test (ANT) specifically in orienting domain. Furthermore, activation of the right PPC had a destructive effect on the top-down attentional control required for selective attention measured by the Stroop test. Also, activation of the right PPC did not affect shifting attention, measured by shifting attention test, and response inhibition, measured by go/ no-go test, which means activation of the right PPC can improve bottom-up attentional control (Salehinejad, Ghayerin, Nejati, Yavari, & Nitsche, 2020).

Deep Transcranial Magnetic Stimulation (dTMS) study. Individuals with ADHD under treatment by dTMS have shown improvement on the N-back task by increasing activation on the right parietal cortex and other areas, measured by fMRI (Bleich-Cohen et al., 2021).

Table 1. Main characteristics of fMRI studies investigating the role of the parietal lobe in ADHD

Authors (year)	Group: n (mean age ± SD, range in year); gender (m/f)	Results
Salmi et al., (2020)	ADHD: 51 (31 ± 9, 19–56), 24/27 TD: 29(33 ± 8, 19–50), 12/17	Intersubject correlations in the parietal cortex were weaker during irrelevant speech or music in a cocktail-party condition
Jiang et al. (2019)	ADHD: 30 (9.2 ± 1.7, 7–13), 14/16 TD: 51 (9.7 ± 1.8, 7–13), 15/18	Decreased degree of centrality values in the RIPL gyrus
Wang et al. (2019)	ADHD: 119 (10.2 ± 1.8,7–14), 80/30 TD: 69 (10.2 ± 1.9, 7–14), 33/36	More decentralized organization in the FPA
Berberat et al. (2021)	MED-ADHD: 15(38 ± 8, 21–58), 3/12 none MED-ADHD: 15(43 ± 8, 29–56), 8/7TD: 15(38 ± 12, 22–55), 3/12	More activation on BIPL during Stroop task and less activation in the LPL during switch task
Kolodny et al. (2020)	ADHD: 37(26.6 ± 4.0, 19–34), 15/22	Increases FP connectivity during Go/ No-Go task
Lindholm et al. (2019)	ADHD: 23 (22.7 ± 0.6, 16-18), 17/6 TD: 29 (22.9 ± 0.9, 16-18), 23/6	Increased activity in LIPL during viewing fearful face
Bachmann et al. (2018)	ADHD-MAP: 21 (40 ± 10.58, 18-65), 8/13 ADHD-PE: 19 (40.26± 13.81, 18-65), 10/9	Higher activation of the BIPL and right precuneus during working memory task
Schulz et al. (2017)	ADHD:27(24.2± 1.9),24/3 TD: 28 (24.6± 2), 24/4	Lower activation of PL during cognitive control tasks
Lin et al. (2015)	ADHD: 39 (9.94 ± 1.77, 7-14), 34/5 TD: 31 (10.04 ± 2.13, 7-14, 25/6	Weaker connectivity between the LAPFC and the RIPL lobe during continuous performance task
Bush et al. (2013)	ADHD-ATMX*:*11 ADHD-MFD*:*11 ADHD-P*:* 10	Treatment by ATMX was associated with increased activation of PL

Schwerdtfeger et al. (2013)	ADHD: 14 (29.5 ± 9.4) TD: 14 (29.6 ± 9.6)	Less activation in the PEF during antisaccade task
Ko et al. (2013)	ADHD: 20 (25.35 ± 2.06), 20/0 TD: 20 (26.30± 1.84), 20/0	Decreased brain activation over the left precuneus and greater decrease in brain activation over the LFPN
Massat et al. (2012)	ADHD: 19 (10.75±1.31, 8-12), 9/10 TD: 14 (10.05±1.28, 8-12), 8/6	Decreased activity in BIPL during N-Back test
Schneider et al. (2010)	ADHD-combined: 11(32.6±9.4, 19-48), 6/5 ADHD-remitted: 8(32.4±8.3, 18-45), 7/1 TD:17 (29.4±8.6, 18-45), 10/7	Reduced activity in the PLduring continuous performance test

Note: ADHD: attention deficit- hyperactivity disorder, TD: typically developing,MED: medication, MAP:mindfulness awareness practice, PE: versus psychoeducation, BSPL: bilateral superior parietal lobule, LIPS: left intraparietal sulcus, RIPL: right inferior parietal lobe, FPA: frontal-parietal attention network, BIPL: bilateral inferior parietal lobe, LPL: left parietal lobe, FP: fronto-parietal, LIPL: left inferior parietal lobe, PL: parietal lobe, LAPFC: left anterior prefrontal cortex, ATMX: atomoxetine, PEF: parietal eye fields, LFPN: left fronto-parietal network.

Table 2. Main characteristics of sMRI, MPRAGE, EEG, tDCS, and TMS studies investigating the role of the parietal lobe in ADHD

Authors (year)	Method	Group: n (mean age ± SD, range in year); gender (m/f)	results
Vilgis et al. (2016)	sMRI	ADHD: 48(12.58 ± 2.21, 8-17.5), 48/0 TD: 31(12.75±1.96, 8-17.5), 31/0	Lower global and local grey matter volumes of RPL in ADHD
Jacobson et al. (2018)	MPRAGE	ADHD: 52(5.01±0.58), 4-5 TD: 38(4.92±0.58), 4-5	Widespread cortical volume reductions in the PL
Juurmaa et al. (2020)	EEG	ADHD: 53(36.26 ± 10.2, 18-60), 25/28	Less PL theta rhythm and more alpha rhythm ERS during inhibition and response and less FP connectivity

		TD: 18(32.78± 10.82, 18-60), 25/28	
Chen et al. (2021)	EEG	ADHD: 40 (7.65 ± 2.11), 35/5 TD: 31(7.68 ± 2.36) ;(20/11)	Less TFP connectivity during oddball task
Salehinejad et al. (2020)	tDCS	ADHD: 17 (9.53 ± 1.5), 12/5	Activation of the RPPC had a destructive effect on the TDAC & has no effect on shifting attention and response inhibition & improves BUAC
Bleich-Cohen et al. (2021)	dTMS & fMRI	ADHD-rPFC: 24 (35.6 ± 8.7, 18-60), 17/7 ADHD-lPFC: 22 (35.1 ± 10.1, 18-60), 15/7 Sham: 16(34.7 ± 9.2, 18-60), 8/8	Activation of the RPL and other areas improve WM

Note: ADHD: attention deficit- hyperactivity disorder, TD: typically developing, RP: right parietal lobe, PL: parietal lobe, FP: fronto- parietal, TFP: temporal and frontal and parietal, RPPC: right posterior parietal cortex, RPL: right parietal lobe, TDAC: top-down attentional control, BUAC: bottom-up attentional control, WM: working memory.

Discussion

The present study aimed to review the role of the parietal cortex in the psychopathology of ADHD. The results of the reviewed studies with different methods, 14 fMRI studies and one sMRI study, one MPRAGE study, two EEG studies, one tDCS study, and one dTMS study, identified abnormal structure, and function in the parietal lobe in individual with ADHD. In the following section, abnormal structure and function of the parietal lobes were discussed in detail.

The right parietal lobe. In the included studies, a resting-state fMRI study showed decreased degree of centrality in the right IPL (Jiang et al., 2019). The reduced activity of the right IPL has been found during continuous performance test (Lin et al., 2015). The right IPL, as a part of the default mode network (DMN), is impaired in individuals with ADHD (Jiang et al., 2019; Lin et al., 2015). The deficient DMN is associated with a wandered mind, which drown individuals with ADHD in daily dream. Furthermore, the mind wandering could be considered as a cognitive underpinnings for ADHD symptoms (Lanier, Noyes, & Biederman, 2019). Furthermore, the right IPL is a part of posterior attention networks which sub serve impaired alerting and orienting attention in individuals with ADHD (Bush, 2010, 2011; Corbetta, Patel, & Shulman, 2008; Malhotra, 2020; Schneider et al., 2010). Moreover, memory and inattention problems are associated with hypo-activation in the right precuneus and parietal lobe (Bachmann et al., 2018; Bleich-Cohen et al., 2021). Although correlational evidence from imaging studies found an association between hyper activation of the right parietal cortex and executive control (Schulz et al., 2017), the causal evidence form stimulation studies did not confirm this association (Salehinejad et al., 2020).

The left parietal lobe. The activity of left IPL decreased during cocktail-party condition (Salmi et al., 2020) and switching task (Berberat et al., 2021), but increased during fearful face mimicry (Lindholm et al., 2019). The left parietal region is not only involved in the obvious symptoms of ADHD, such as inattention, impulsivity, and hyperactivity but also working memory and emotional perception such as fear and happiness. Less activation of the left SPL has a relationship with impulsivity and hyperactivity and inattention in individuals with ADHD and previous studies described the role of this part in shifting attention (Berberat et al., 2021; Schneider et al., 2010). Given the impaired social cognition in individuals with ADHD (Bora & Pantelis, 2016), increasing the activity of the left IPL associated with the left TPJ improves impaired social cognition (Lindholm et al., 2019). Also, impaired working memory in children with ADHD can be attributed to the hypoactivity of the left parietal lobe (Ko et al., 2013). Thus, it seems that this lobe plays a key role in emotional processing, while the right parietal lobe has more prominent role in the processing of basic emotional states. In general, the function of this lobe seems to be more general than the right parietal lobe and this indicates the increasing specialization of the right parietal lobe versus the left parietal lobe.

Bilateral & central parietal lobe. In the included studies, fMRI results described a reduction in bilateral parietal lobe during cocktail-party condition (Salmi et al., 2020), cognitive control task (Schulz et al., 2017), continuous performance test (Schneider et al., 2010). This findings confirmed by MPRAGE, which described a reduction in the volume of the parietal lobes (Jacobson et al., 2018). Furthermore, decreased activity of parietal lobes described through EEG (Cowley et al., 2020). Finally, interventional studies confirm these findings. In children with ADHD, Atomaxitine increases the activity of the parietal lobe (Bush et al., 2013), anodal tDCS improves working memory performance (Salehinejad et al., 2020), and dTMS increases the activity of the right parietal lobe and improved working memory performance (Bleich-Cohen et al., 2021). Lower connectivity of the IPL and the PPC is associated with the ADHD symptoms, which associated with weakness in the control of irrelevant auditory and visual stimuli and inattention symptoms (Chen et al., 2021; Kolodny et al., 2020; Salmi et al., 2020; Schneider et al., 2010; Schwerdtfeger et al., 2013). Functionally, based on EEG results, less theta rhythm and more alpha rhythm are shown during control of irrelevant visual stimuli (Bush et al., 2013; Cowley et al., 2020). However, boosting the right PPC through tDCS did not alter cognitive control (Salehinejad et al., 2020), so it is likely that increased the right parietal cortex activity depends on increased left parietal cortex activity during irrelevant stimulus inhibition, indicating the role of bilateral parietal lobes in cognitive control (Berberat et al., 2021). Also, memory problems are associated with less activation of the bilateral IPL (Bachmann et al., 2018).

Along with reduced interaction and activity, a reduction of the cortical volume of the parietal lobe, is obvious in individuals with ADHD (Jacobson et al., 2018; Massat et al., 2012; Wang et al., 2019). With respect to these results, with a therapeutic approach, increase the activity of the parietal lobes and training of respective functions should be taken into account in rehabilitation of ADHD.

Conclusion

According to the included studies, there is an association between abnormal parietal structure and function and cognitive dysfunction in individuals with ADHD. The impaired structure and function of the parietal lobe could be followed in the activity, size, connections, and processes of this cortex. A variety of cognitive domains, including attention, working memory, inhibitory control, social cognition, and inner thinking, are controlled by the parietal cortex, which impaired in individuals with ADHD. Functional and structural alteration of parietal cortex has been described in ADHD, which have a causal relationship with cognitive impairments. In sum, all included studies described abnormal structural, functional, or connectivity of parietal lobe or improvement of cognitive functions with stimulation of parietal lobe. Some limitation should be taken into account in the present study. The heterogeneity of the tasks which used in the included studies and the variety of methods did not allow us to perform a meta-analysis.

Conflict of interest

The authors acknowledge that there is no conflict of interest and this study was performed with personal grant of the authors.

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