Developmental Cognitive Neuroscience 69 (2024) 101438

Contents lists available at ScienceDirect

Developmental Cognitive Neuroscience

journal homepage: www.elsevier.com/locate/dcn

A comprehensive systematic review of fMRI studies on brain connectivity in healthy children and adolescents: Current insights and future directions

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A R T I C L E I N F O

Keywords:
FMRI
Resting state
Brain connectivity
Functional connectivity
Development
Neurodevelopment
Children
Adolescent

A B S T R A C T

This systematic review considered evidence of children's and adolescents' typical brain connectivity development studied through resting-state functional magnetic resonance imaging (rs-fMRI). With aim of understanding the state of the art, what has been researched thus far and what remains unknown, this paper reviews 58 studies from 2013 to 2023. Considering the results, rs-fMRI stands out as an appropriate technique for studying language and attention within cognitive domains, and personality traits such as impulsivity and empathy. The most used analyses encompass seed-based, independent component analysis (ICA), the amplitude of the low frequency fluctuations (ALFF), and fractional ALFF (fALFF). The findings highlight key themes, including age-related changes in intrinsic connectivity, sex-specific patterns, and the relevance of the Default Mode Network (DMN). Overall, there is a need for longitudinal approaches to trace the typical developmental trajectory of neural networks from childhood through adolescence with fMRI at rest.

1. Introduction

Infancy and adolescence are key periods in the process of neurodevelopment and the emergence of cognitive alterations and psychopathologies (Wainberg et al., 2022). In recent years, brain connectivity studies have noticeably raised great interest as more sophisticated techniques have arisen with promising results. Functional magnetic resonance imaging (fMRI) is currently considered the gold standard for registering brain signals (Welvaert and Rosseel, 2014). Its application to the analyses of brain connectivity at rest has proven to be the valuable choice to unveil intrinsic connections of the brain in the absence of exogenous inputs, referred to as resting-state fMRI (rs-fMRI) (Li et al., 2019). Essentially, rs-fMRI analyses intrinsic, spontaneous, low-frequency fluctuations in the fMRI blood oxygen level-dependent (BOLD) signal that define specific networks without performing any task (Biswal, 2012; Lv et al., 2018). When working with paediatric populations, rs-fMRI is particularly relevant because (a) it equalizes the measure conditions in an absolute manner as it removes the influence of individual differences derived from the performance of a task and the personal competencies of each person, and (b) data acquisition is relatively easy and fast, therefore requiring less participant collaboration (Bernal, 2022; Whitfield-Gabrieli et al., 2020).

A substantial body of evidence points to neurodevelopment as the stage when risk and resilience established to the later onset of

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https://doi.org/10.1016/j.dcn.2024.101438
Received 19 March 2024; Received in revised form 7 August 2024; Accepted 13 August 2024
Available online 15 August 2024

neuropsychiatric illnesses (Solmi et al., 2022). Some authors even allude to sensitive and critical moments that influence brain maturation (Levitt and Veenstra-VanderWeele, 2015). As observed in the literature, the prediction power yielded from intrinsic functional connectivity is one of the most explored applications of rs-fMRI for estimating cognitive functions and states (Agcaoglu et al., 2022; Whitfield-Gabrieli et al., 2020; Zhang et al., 2023). However, this evidence is disaggregated and so far, there has been no undoubted approach that allows us to speak conclusively of a biomarker role of the connectivity networks with fMRI signals at rest.

A complementary line of research proposes a different perspective for the exploration of rs-fMRI signal. This one advocates for overcoming the comparative studies of different levels of cognitive impairment, and progress towards modelling how the process of brain complexity in connectivity networks occurs by studying this process at the same time as the process of healthy neurodevelopment. Some studies have followed this approach, concluding that age-related changes in connection strength are specific to neurodevelopmental stages (Içer, 2019; Teeuw et al., 2019). Also, functional specialization of brain networks apparently increases with age (Lei et al., 2022). However, the studies focusing on identifying normal brain development within a young population are scarce.

Considering that significant changes in the functional development of the brain occur between childhood and adolescence, the breakdown of age-related changes along the process of brain maturation provides meaningful information (Liu et al., 2023). Thereby, we consider the use of functional connectivity measures derived from rs-fMRI to be well justified in studying age-related changes and brain maturation about the wiring of neural networks and brain complexity. There have been attempts to explain the resting state connectivity through fMRI, such as the review proposed by Zhang et al. (2019), however, to our knowledge, no research has reviewed this in healthy youth exclusively.

Given the aforementioned points, it seems clear that applying rs-fMRI to the analysis of healthy children and adolescents may provide an opportunity to disclosure the developmental neurobiology both as a baseline and as a comparison point of underlying neurodevelopmental disorders. In the last ten years, attempts have been made to establish the relation between the properties of connectivity networks and certain psychological variables or variables derived from neuropsychological performance (Figueroa-Jiménez et al., 2021; Guàrdia-Olmos et al., 2022; Haghighat et al., 2021; Whitfield-Gabrieli et al., 2020). The fundamental issue is to identify a regular and systematic basis within this relation and to extract utilities of an applied nature. Ultimately, the question remains to know which of the indicators that characterize a brain connectivity network at rest with fMRI signal can be used as indicators of cognitive states or situations of health or pathology, as it is demonstrated in an incipient way. To do so, it is necessary first to tackle the challenge of modelling how this process of complexity in brain connectivity occurs regarding the process of brain maturation. Here is where our systematic review may help fill in the gap in the literature. The present work participates in the current efforts to pool resources and data across multiple sites and investigations with hopes that this will shed light on addressing clinical developmental questions.

Hence, our proposal with this systematic review is to delve into the present knowledge of brain connectivity in healthy children and adolescents as studied through fMRI technique. This systematic review will help elucidate changes in brain connections underlying cognitive development, as it will provide a detailed connectome theory of child and adolescence neurodevelopment to guide physiological and clinical lines of research in this topic.

2. Methods

A systematic review adhering to the PRISMA guidelines was undertaken (Page et al., 2021). Articles included in this study were sourced from the Web of Science (WoS), PubMed, and PsycInfo databases to identify articles published between 2013 and September 2023. The literature search employed a Boolean algorithm combining the following keywords: ("fMRI" OR "functional magnetic resonance imaging") AND ("children" OR "adolescents" OR "youth" OR "child" OR "teenager") AND ("resting state" OR "rs-fMRI") within the title or abstract of the papers.

Three researchers independently searched, resulting in a total of 3421 studies and reaching 100 % of agreement. The search yielded 1463 papers from the WoS database, 1260 from PubMed, and 698 from PsycInfo. We applied the following inclusion criteria: (a) children and adolescents ranging from 3 to 20 years old, encompassing early childhood to late adolescence; (b) healthy or typically developing (TD) individuals; and (c) measurement of brain signal through fMRI during resting state.

The exclusion criteria were as follows: (a) history or current diagnosis of a psychiatric or neurodevelopmental disorder; (b) history or current presence of serious medical conditions that deviate from the normal development; (c) parental history of major psychiatric or neurological disorders; (d) parent-reported prenatal exposure to alcohol or drugs; (e) task-based approaches; (f) a different brain recording technique besides fMRI; (g) systematic reviews, meta-analysis, thesis or clinical essays; (h) animal population; and (i) studies focused on the impact of socioeconomic conditions, poverty and parental neglect on brain signals; (j) information about fMRI is incomplete. For example, statistical analysis, brain areas, coordinates, or analysis strategy (ALFF, fALFF, ReHo) are not specified. Relevant information from each article was entered into a spreadsheet, covering: (1) sample characteristics, detailing the population type (healthy or TD), sample size, gender, and age; (2) resting time during fMRI; (3) established comparisons; (4) study design; (5) signal analysis; (6) examined brain areas; and (7) main findings.

Following the process of deduplication across the databases, 1819 duplicate records were removed with the help of Rayyan. Subsequently, all articles underwent three rounds of screening by three independent reviewers (RCG, MGTM, CK). The initial level of agreement was of 92 % and they concurred the decision to include or discard the articles on which there was a conflict. At this point, 1424 studies were excluded during title/abstract screening due to non-compliance with the inclusion criteria. After the screening process, 178 articles remained to follow to eligibility step. During the eligibility process, 120 studies were excluded due to inconsistencies with the inclusion criteria after the full text had been reviewed. In this step, the three reviewers reached an initial level of agreement of 93 %. Discrepancies between reviewers that were related to article eligibility were presented to the study team and a consensus was reached through discussion. As a result, the final sample comprised 58 papers, which carries the symbol * in the bibliography. Fig. 1 provides a visual summary of this search process.

3. Results

Age along the sample range is between 3 and 20 years, encompassing early childhood through late adolescence. Since they are working with healthy TD youth, many studies lack a control group. In fact, in 32 studies there is no comparison between groups. Among the studies that compare groups, ten make comparisons between different age groups, five compare a group that does some physical exercise vs a control group, four compare girls and boys, three compare a group that receives cognitive training vs a control group, one study compares risk-taking individuals vs non-risk-taking individuals, one compares participants with high MAOA genotype vs low MAOA genotype, one compares a group of positive hypothalamus-pituitary-gonadal and a group of negative hypothalamus-pituitary-gonadal, and another one compares monolingual vs multilingual persons. Regarding the type of study performed, the vast majority of them are cross-sectional –50 studies- while only eight are longitudinal. The percentage of males and females, in general, is similar. There are two studies whose sample consist of only males (Ge et al., 2021; Lei et al., 2014) and only one study has

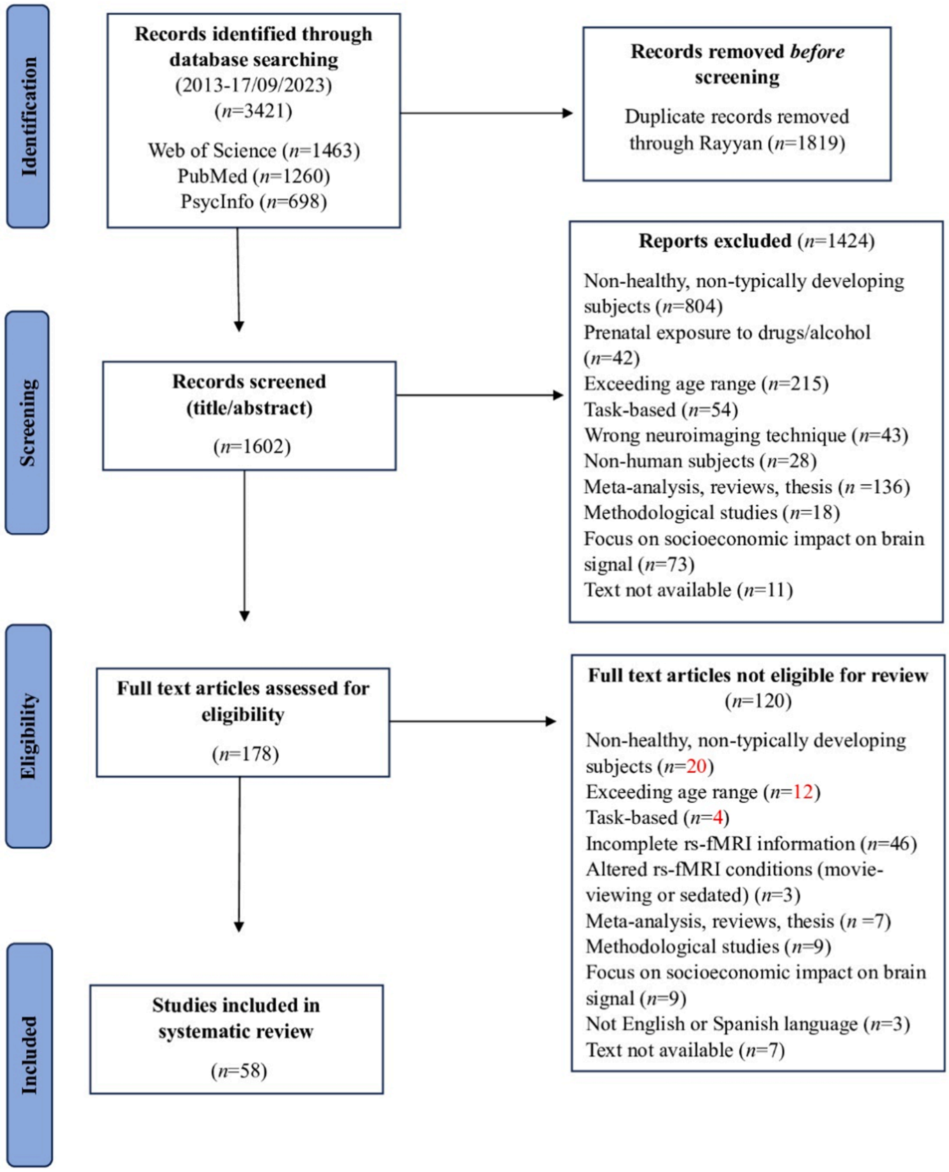

Fig. 1. Flowchart of the systematic review search conducted.

exclusively females as participants (Xie et al., 2019). Sample sizes are moderate in most cases and lie beneath a hundred participants. The smallest sample had 10 participants (Wang and Huang, 2021). Nonetheless, there are a few studies that have broader sizes where we can highlight Sato et al., (2014) with 229 individuals. All these resting-state studies were based on imaging sequences that ranged from 5 to 12 minutes in duration. Among the methods to measure the rs-fMRI signal, the most popular one in this review is seed-based analysis, which was performed in 26 papers. It is followed by an independent component analysis (ICA) used in eight papers, amplitude of low-frequency fluctuations (ALFF) and fractional ALFF (fALFF) used in six and four articles respectively, regional homogeneity analysis (ReHo) in four papers, and several measures of graph theory that were applied to three articles.

3.1. Sex differences

The reviewed studies highlight significant sex differences in brain connectivity and cognitive development. Alarcón et al. (2015) reported developmental sex differences in the amygdala's resting-state functional connectivity with parieto-occipital regions during adolescence, revealing distinct patterns for each sex. Içer et al. (2020) found that boys and girls with ADHD exhibit different patterns of cortical thickness and surface area, indicating sex-specific neural underpinnings. Lee et al. (2023) identified sex differences in brain structural covariance networks across the lifespan, suggesting that males and females have distinct brain network organizations influencing cognitive and behavioural outcomes. Liang et al. (2022) observed that visual network connectivity strengthens with age in girls, implying a sex-specific trajectory in reading skill development. Lastly, Yoon et al. (2022) showed that boys and girls have different patterns of intrinsic brain connectivity associated with externalizing behaviours, further emphasizing the role of sex differences in brain function and behaviour. These findings underscore the importance of considering sex as a critical factor in neurodevelopmental research.

3.2. Cognitive domains: a developmental view

Language seems to be the most widely studied process in early childhood. Indeed, nearly all papers that target the first years of infancy

–around 3 years-old– address the neural basis of language acquisition and processing through resting-state functional connectivity (rs-FC) (Manning et al., 2022; Thieba et al., 2019; Xiao, Friederici, et al., 2016). Xiao, Brauer, et al., (2016) compared a group of TD 3-years-old and a group of TD 5-years-old and observed an increased left lateralization in the connectivity of the posterior superior temporal gyrus (PSTG) and inferior frontal gyrus (IFG). Similarly, Xiao, Friederici, et al. (2016) worked with 5- and 6-years old children and they identified that enhanced connectivity between left PSTG and bilateral IFG were associated with greater language abilities with age. Reading skills have been studied as early as 3 years old by Manning et al. (2022), who observed that increased connectivity between the Frontoparietal Language Network (FPLN) and Default Mode Network (DMN), and between occipital Visual Network (VN) and FPLN could predict phonological processing a year later. Alcauter et al. (2017) also focused on reading and with slightly older children (6–9 years old) they also identified high activity in prefrontal regions, as well as the temporal cortex, as predictors of reading skills, specifically, reading speed.

Attention garners heightened scrutiny in studies centred around late childhood. Two studies during this period report changes in attention related to frontal areas. Whitfield-Gabrieli et al. (2020) found an association between lower activity in medial prefrontal cortex (MPFC) and dorsolateral prefrontal cortex (DLPF) and better attention four years later. With a similar age sample, Sánchez-Pérez et al., (2019) showed that children undertaking an attention and working memory program exhibited higher connectivity within the middle frontal gyrus (MFG) and between the right MFG and parietal regions. Meri et al. (2023) focused on screen exposure and concluded that higher access to screens was related to lower FC between resting-state networks (RSN) associated with basic attention skills and cognitive control. Another main cognitive domain that begins to draw attention during this developmental stage is reasoning. Two papers analysed abacus-based mental calculation (AMC) training, a specific mental calculation skills. The one conducted by Zhang et al. (2021) delved into the adaptative configuration of brain modular organization, specifically, through the plasticity of community structure –in brief, how nodes within the network divide into modules-. They described greater segregation in AMC group. For their part, Jia et al. (2021) identified a positive correlation between the rostrolateral prefrontal cortex (RLPFC) and reasoning skills in the children trained with the AMC. Li and Tian (2014) had previously obtained similar results, highlighting the Prefrontal Network (PFN) as the key region for intelligence quotient.

During the period of early adolescence, there is a lack of studies to understand the rs-FC underlying specific cognitive domains in healthy youth. For the most part, the transition to early adolescence generates interest towards personality traits. We only included one study in this review, by Liang et al., (2022) where tackled sex differences in reading.

Lastly, out of the three studies on late adolescence, only one regards the cognitive domain of learning and motivation. It is the one conducted by Wang et al. (2017) and they analyse motivation and reward through a component of self-regulation, delay-discounting, which refers to the tendency to prefer smaller-but-sooner rewards over larger-but-later rewards. They found that delay-discounting was associated with greater connectivity in the dorsal anterior cingulate cortex (DACC), and between DACC and the left DLPFC.

3.3. Emotional regulation

Another topic of research in early childhood is emotional regulation and its intrinsic correlates. Liuzzi et al. (2023) described irritability in 4- to 6-year-old children where irritability level positively correlated to connectivity between the amygdala and posterior cingulate. Irritability also predicted decreases in intrinsic connectivity as children aged between amygdala, and frontal and parietal regions. For their part, Correia et al., (2019) studied emotional prosody recognition in 7- to 9-year-old children, finding a stronger connectivity between IFG and motor regions enhances emotion recognition.

3.4. Personality traits

Personality traits were widely studied in our included papers. Impulsivity is considered to be a personality trait, even though some authors measure it through a temperament questionnaire (Inuggi et al., 2014). Both impulsivity and risk-taking seem to be supported by hyperactivation in regions appertaining the DMN (DeWitt et al., 2014; Inuggi et al., 2014). Li et al. (2020) described the propensity to aggressiveness in children as a personality trait characterized by hypoactivity within the left superior temporal gyrus (STG), the right parahippocampal gyrus (PHG) and the left supramarginal gyrus (SMG). Additionally, Lei et al. (2014) discovered the MAOA gene as a regulator in the association between impulsivity and activity in pons exclusively in male adolescents.

Five studies concerned empathy. Three of them focus on callous-unemotional trait (CU), a personality trait defined as an impairment in prosocial emotions of guilt, remorse and empathy that implies restricted affect and a lack of concern for performance. It seems clear that CU and both cognitive and affective empathy do not share the same intrinsic connections (Winters et al., 2022; Winters and Hyde, 2022). Cognitive empathy associated with increased DMN activity and both cognitive and affective empathy correlate to hyperactivity between DMN and Salience Network (SN) (Winters and Hyde, 2022; Winters, Pruitt et al., 2021). In contrast, CU associated to decreased DMN activity (Winters and Hyde, 2022). In the same year, Winters et al. (2022) found that CU moderates the association between DMN and Frontoparietal Network (FPN) –the neural correlates of empathy- in adolescents. Winters, Sakai et al. (2021) followed a different perspective by analysing the heterogeneity network features in RSN and observed that low density in the FPN and high density in DMN and FPN are beneath CU. In a younger population, empathy creates a distinct pattern of activation for affective empathy and cognitive empathy: affective empathy relates to weak activation of the DMN, whereas cognitive empathy associated to connectivity between dorsolateral DMN with pre- and postcentral gyrus.

3.5. Brain areas and networks

The most frequently reported network was the DMN, which was the focus of 12 studies. This network appears to be crucial during early childhood, as it experiences a significant strong development from 3 to 5 years of age (Li et al., 2019; Xiao, Zhai et al., 2016). Furthermore, the DMN –as well as the Executive Control Network (ECN)- is extremely important during the period of 7–15 years old, characterized by the integration between its anterior and posterior nodes and the rise in degree centrality (DC) of the hubs (Sato et al., 2014). We must highlight the role of the hyperactivation of DMN in the presence of impulsivity in children, as revealed by Inuggi et al. (2014). Moreover, this network has a key role in the development of empathy and callous-unemotional traits (Bray et al., 2022; Winters et al., 2022; Winters, Pruitt, et al., 2021; Winters, Sakai, et al., 2021; Winters and Hyde, 2022).

Regarding the Attention Network (AN), it is worth mentioning its role in explaining variations in the levels of subclinical depressive symptoms. According to Liu et al. (2019), stronger connections between the ventrolateral prefrontal cortex (VLPFC) and left temporoparietal junction (TPJ) within the ventral AN was associated with higher scores in subclinical depressive symptomatology for TD adolescents. This network benefits from cognitive training programs as the one proposed by Sánchez-Pérez et al. (2019) and the screen exposure negatively affects AN (Meri et al., 2023). Exploration of the AN appears in eight studies.

FPN was studied in eight papers. It was proved to have key roles in the development of conscientiousness personality trait in children (Yi et al., 2023) and in intelligence for children and adolescents (Li and Tian, 2014). Also, FPN reorganization in healthy children may act as an underlying mechanism between cardiovascular fitness and gross motor skills with neurocognitive functioning (Meijer et al., 2022b).

SN was explored in seven studies, however, only one obtained noteworthy results regarding SN. Geng et al. (2015) identified inter and intra-hypoconnectivity in the SN as the neural underpinning of anxiety trait. The insula, a remarkable brain region appertaining the SN, is associated with intolerance of uncertainty personality traits. Youth with high intolerance of uncertainty shows stronger positive connectivity between the anterior insula and frontal regions, and negative connectivity within the SN (DeSerisy et al., 2020).

VN mainly supports reading skills, with a sex-specific pattern of activity: VN connectivity strengthens with age only for girls (Liang et al., 2022; Manning et al., 2022). VN seems to follow a path of decreasing connectivity with age in the transition from childhood to adolescence (7–15 years old) (Sato et al., 2015). Also, it is affected by combat sports by increasing FC within the cerebellum (Kim et al., 2015; Li et al., 2021), even though Li et al. (2022) found a more specific effect, reducing connectivity in inferior regions of the cerebellum, while increasing superior areas (Li et al., 2022).

ECN was reported in four papers, but only one of them obtained substantial results for this network. Chahal et al. (2021) describe that youth in more advanced stages of puberty showed increased internalizing symptoms during the COVID-19 pandemic only if their ECN was below average, suggesting the role of ECN in protecting against risk factors. Sensorimotor Network (SMN) seems to foster the effects of physical activity and sports on intrinsic connectivity (Li et al., 2021; Meijer et al., 2022b) and cognitive training (Zhang et al., 2021). It is mentioned in four articles.

In addition, specific brain regions were the focus of some studies. Amygdala was identified as an important area in adolescents for a tendency to risk-taking behaviours (DeWitt et al., 2014) and subclinical depressive symptomatology and negative affect (Ge et al., 2021). Alarcón et al. (2015) report immaturity of amygdala rs-FC with parieto-occipital regions during adolescence, with unique patterns in both sexes. The strength of hippocampus activity with regions of lateral temporal lobes and ACC increases with age between 4 and 10 years old (Blankenship et al., 2017). For their part, Thomason et al. (2013) demonstrate for the first time that the FC of the hippocampus is altered with changing cortisol levels.

3.6. *Hemispheric asymmetry*

Several studies in our review addressed the topic of hemispheric asymmetry, particularly in relation to language development and reading skills. Alcauter et al. (2017) investigated functional connectivity in children aged 6–9 years and found that the lateralization of connectivity in the prefrontal cortex and Broca's area is associated with reading skills. Similarly, Xiao, Brauer et al. (2016) compared 3- and 5-year-old children and observed increased left lateralization in the connectivity of the posterior superior temporal gyrus (PSTG) and the inferior frontal gyrus (IFG), which is related to language development. Further, Xiao, Zhai et al. (2016) examined children aged 3–6 years and found left lateralization of connectivity in areas associated with language processing, such as the PSTG and IFG. Additionally, Liang et al. (2022) explored sex differences in the connectivity of the visual network and reported that the lateralization of connectivity in this network varies with age in girls, suggesting a sex-specific pattern in the development of reading skills. These findings underscore the significance of hemispheric asymmetry in the cognitive development of language and reading abilities during childhood and adolescence.

A summary of the results found in the different works is provided in Table 1.

4. Discussion

This study aims to analyze rs-fMRI studies from the past decade to understand the developing brain in children and adolescents. Population aged 3–20 years were included, but varying sample sizes and lack of control groups pose challenges. Standardized protocols are needed for better comparison among studies. Many psychiatric disorders start early in life, with 50 % of the projected lifetime risk of developing a mental disorder is already accumulated (Jones, 2013). Previous findings state that neuropsychiatric disorders are deviations from typical neurodevelopmental trajectories (Sato et al., 2016; Wainberg et al., 2022). Therefore, understanding healthy brain connectivity early on is crucial for detecting abnormal trajectories and improving diagnoses and early intervention strategies.

Multiple studies (Alarcón et al., 2015; Içer et al., 2020; Lee et al., 2023; Liang et al., 2022; Yoon et al., 2022) in our sample explored sex differences, revealing age-dependent modulation and unique neural mechanisms predicting psychopathology changes. Liang et al. (2022) focused on reading-related neural networks, showing increased connectivity strength in girls over time, while Lee et al. (2023) examined sex-specific markers for internalizing and externalizing problems. Alarcon et al. (2015) studied age-sex interactions on amygdala connectivity, and Yoon et al. (2022) investigated personality traits' associations with brain connectivity. These findings stress the importance of sex-specific neural patterns in understanding brain development, emphasizing age-related modulation, DMN involvement, behavioral correlations, and sex-specific connectivity patterns.

Around five years of age there is a significant strengthening of intrinsic connectivity, especially in the DMN (Dai et al., 2019; Li et al., 2019; Xiao, Zhai et al., 2016). The three of them compare 3 years old to 5 years old. In particular, the DMN undergoes a strengthening in its development at 5 years of age (Li et al., 2019; Xiao, Zhai et al., 2016). Subsequently, the DMN experiences an increasing integration between the anterior and posterior neural nodes, along with enhanced DC in the neural hubs during the period of 7–15 years old (Sato et al., 2014). Nonetheless, investigation on the typical development of the DMN during adolescence seems to slow down.

Longitudinal studies provide important information but often cover short ages ranges, missing crucial developmental stages. For instance, a year between the first time point and the second time point in the case of Xiao, Friederici et al. (2016) or a maximum of six years gap at Chahal et al. (2021). Hence, they encompass only one developmental stage in most cases. Short-term longitudinal studies often fail to fully harness the potential inherent in exploring neurodevelopment, given the intricacies of brain complexity. To complete the age range from 3 to 20 years, there remains a need for studies focusing on early adolescence, middle adolescence, late childhood, and the latter half of the teenage years. In this context, the longitudinal studies by Fan et al. (2021), Simmonds et al. (2017), and Szaflarski et al. (2012) provide crucial insights into dynamic developmental trajectories of neural systems. Simmonds et al. (2017) examine the maturation of working memory over 9 years, revealing shifts from executive systems to specialized regions. Szaflarski et al. (2012) explore the 10-year developmental trajectory of narrative processing, showing a linear increase in bilateral superior temporal cortical activation. Fan et al. (2021) depict developmental patterns of the DMN, indicating increased connectivity strength and spatial convergence with young adults. These studies highlight the importance of longitudinal designs in understanding the complexities of cognitive and neural development across childhood and adolescence.

The developmental trajectory of cognitive domains, as revealed through resting-state functional connectivity (rs-FC) studies, underscores the evolving neural underpinnings of language, reading, attention, reasoning, and motivation across childhood and adolescence. Language acquisition and processing are prominently investigated in early childhood, with studies highlighting increased left lateralization in connectivity between regions like the posterior superior temporal gyrus (PSTG) and inferior frontal gyrus (IFG) as predictive of language abilities (Xiao, Brauer, et al., 2016; Manning et al., 2022). Reading skills, examined as early as age 3, show associations between enhanced

Table 1
Major characteristics of the studies included in the systematic review.

ID	Population (n)	% male	Age studied Range (mean, standard deviation)	Resting duration time	Comparison groups	Design	Analyses	Brain regions examined	Main findings
Agcaoglu et al., (2022)	TD children (n=124)	NR	8–17 (12.6)	5'	NR	Longitudinal, two timepoints	ICA	Subcortical Networks, AUN, SMN, VN, DMN, Cognitive Control Network, CEN	Decreased spectral power in high frequencies and increased spectral power in low frequencies with age may be a biomarker of typical brain development.
Alarcón et al., (2015)	TD adolescents (n=122)	58.1 % (n=71)	10–16 Girls (13.8 ±1.4) Boys (14.1 ±1.2)	9'	Girls vs. Boys	Cross-sectional	Seed-based analysis	(L)IPL, (R)AG, (L)SFG, (L) Precuneus, (L) Middle occipital gyrus, (L) Postcentral gyrus, (R) Lingual gyrus, (L) VMPFC, (R) Cuneus, (R) Culmen, (R) DMPFC	Amygdala sub-regional RSFC with parieto-occipital cortex decreases with age, and with medial frontal cortex increases. Also, there is a laterality effect that differentiates the sexes: increased coupling of left superficial amygdala with VMPFC for boys, and enhanced coupling of right superficial amygdala with DMPFC for girls.
Alcauter et al., (2017)	Healthy children (n=60)	41 % (n=25)	6–9 (8.46 ±0.77)	5'	NA	Cross-sectional	ICA	(B)SMA, (L)IFG, (L)MFG, (L) Precentral gyrus, (L)ITG, (L)STG, (L)SPL	Functional connectivity of the left frontal and temporal cortex and subcortical regions predict reading speed.
Blankenship et al., (2017)	TD children (n=97)	41.2 % (n=40)	4.02–10.81 (6.68±1.42)	6'	NA	Cross-sectional	Seed-based analysis	(R) Hippocampus, (L)AG, Pons, (B) Precentral gyrus, (L)MFG, (R)MTG	The hippocampus is a highly connected structure of the brain and many of the major components of the adult network are evident in childhood, including both unique and overlapping connectivity between anterior and posterior regions. Furthermore, the strength of hippocampal connectivity with lateral temporal lobe regions and anterior cingulate regions is found to increase with age.
Bray et al., (2022)	TD children (n=120)	48 % (n=54)	9–10 (9.98 ±0.36)	6.18'	NA	Cross-sectional	Seed-based analysis	(B)Insula/IFG, (B)AMCC/ DACC, (B)SMA, (B)Precuneus, (B)STG, (B)SFG	Higher affective empathy is associated with weaker connectivity between key hubs of the DMN and

(continued on next page)

Table 1 (*continued*)

ID	Population (n)	% male	Age studied Range (mean, standard deviation)	Resting duration time	Comparison groups	Design	Analyses	Brain regions examined	Main findings
									other widespread regions in the brain. Higher cognitive empathy is linked to both stronger and weaker connectivity between dorsal and lateral DMN, and pre- postcentral gyrus, and the cerebellum. This indicates more widespread neural correlates of empathy, with less specialization.
Chahal et al., (2021)	Healthy adolescents (n=85)	51 % (n=43)	9–19 (11.29 ±0.92)	6'	9–13 years old (1st timepoint) vs. 13–19 years old (2nd timepoint)	Longitudinal, two timepoints	ICA	ECN	Youth in advanced stages of puberty for their age exhibited abrupt increases in the severity of internalizing symptoms during COVID−19 5 years later. However, this effect was only present in youth with low ECN coherence. Hence, ECN coherence serves as a biomarker for resilience.
Correia et al., (2019)	TD children (n=55)	41.8 % (n=23)	7.75–9.25 (8.31±0.32)	7'30''	NA	Cross-sectional	Seed-based analysis	(B)Precentral gyrus, (R)SFG, SMA, Paracingulate gyrus, (L) Posterior cingulate gyrus	Individual differences in the engagement of sensorimotor systems, and in their coupling with inferior frontal regions, underpin variation in children's emotional speech perception skills. They suggest that sensorimotor and higher-order evaluative processes interact to aid emotion recognition and have implications for models of vocal emotional communication.
Dai et al., (2019)	TD children (n=30)	50 % (n=15)	3-year-old group: (3 ±0.16) 5-year-old group: (5 ±0.16)	8'	3-year-old group vs. 5-year-old group	Cross-sectional	Seed-based analysis	IFG	In this study, a right lateralized mirror neuron system with a positive correlation between the IFG and inferior parietal lobe was identified in both age groups. Spontaneous functional

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Table 1 (*continued*)

ID	Population (n)	% male	Age studied Range (mean, standard deviation)	Resting duration time	Comparison groups	Design	Analyses	Brain regions examined	Main findings
									connectivity of the MNS is formed as early as 3 years of age and shows age-related development in the preschool period.
DeSerisy et al., (2020)	Healthy children and adolescents (n=57)	55 % (n=31)	8–18 (12.56 ±2.86)	6’	NA	Cross-sectional	Seed-based analysis	(B)AI	Whereas Intolerance of Uncertainty Scale for Children (IUSC−12) is not associated with bilateral AI, two subscales are. Youth with higher Inhibitory Intolerance of Uncertainty demonstrated increased activity between AI and right frontal regions. Higher Prospective Intolerance of Uncertainty was associated with decreased FC between AI and anterior cingulate.
DeWitt et al., (2014)	TD adoelscents (n=36)	44.44 % (n=16)	Risk-taking-adolescents: 12–17 (14 ±1.6) Non-risk-taking adolescents: 12–17 (14 ±1.7)	5’	Risk-taking adolescents vs. Non-risk-taking adolescents	Cross-sectional	Seed-based analysis	(B)Amygdala, (B)Nucleus accumbens	Risk-taking behavior in adolescents is associated with hyperconnectivity at rest in networks accounted for emotion regulation, reward sensitivity and executive control.
Ge et al., (2021)	Healthy male adoelscents (n=23)	100 % (n=23)	Acute exercise group: 18–19 (18.18 ±0.39) Control group: 18–19 (18.45 ±0.52)	NR	Adolescents assigned to acute exercise group vs. Control group	Repeated cross-sectional, pre-post	Seed-based analysis	(B)Amygdala	Moderate-intensity acute exercise reduces negative emotions, mainly depression, which is associated with enhanced amygdala-orbitofrontal cortex connectivity.
Geng et al., (2015)	Healthy adolescents (n=60)	53.03 % (n=35)	(15.68 ±1.00)	7’30’’	NA	Cross-sectional	Seed-based analysis	Basolateral amygdala, AI, DACC	Weaker intra and inter-network FC in the SN is associated with higher trait anxiety in adolescents, indicating impaired cognitive control in trait anxiety.
Hehr et al., (2019)	63 children and adolescents	46.03 % (n=29)	6–17 (10.52 ±3.07)	10’	NA	Cross-sectional	ICA	Amygdala, VACC, Precentral gyrus, STG	Both sleep duration and midpoint of sleep are associated with next-day rs-FC within corticolimbic emotion-related neural circuitry in

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ID	Population (n)	% male	Age studied Range (mean, standard deviation)	Resting duration time	Comparison groups	Design	Analyses	Brain regions examined	Main findings
									children and adolescents.
Içer et al., (2020)	Healthy children and adolescents (n=68)	50 % (n=34)	Boys: 7–18 (12.33 ±3.14) Girls: 7–18 (11.88 ±2.97)	6’38’’	Girls vs. Boys	Cross-sectional	ALFF, fALFF, seed-based analysis	DMN, SMN, VN, SN, DAN, FPN, LN, CEN	Girls exhibit higher FC and more developed language and visual functions than boys. Then, gender differences in brain networks should be taken into consideration when examining childhood cognitive status and the results should also be evaluated according to gender.
Içer, (2019)	Healthy children and adolescents (n=53)	45.28 % (n=24)	Late childhood group: 8–9 (8.53±0.56) Adolescence group: 13–14 (13.61 ±0.65) Late adolescence group: 16–18 (16.90 ±0.74)	NR	Late childhood group vs. Adolescence group vs. Late adolescence group	Cross-sectional	Seed-based analysis	DMN, MPFC, PCC, ACC, (B) RPFC, SMG, DAN, SMN, VN, LN, IFG, PSTG, FPN, DLPFC, CEN	FC of the brain restructure during adolescence development and age-related changes in connection strength seem to be specific to developmental stages. FC increases within networks and decreases between networks from childhood to late adolescence.
Inuggi et al., (2014)	TD children (n=19)	56.63 % (n=10)	8–12 (9.9 ±1.4)	6’30’’	NA	Cross-sectional	ICA, seed-based analysis	DMN, ECN, SMN, FPN, VN	Proneness to impulsivity is expressed as a negative association between areas in the DMN and in action-related networks, which constitutes a possible biomarker. This is the first evidence that impulsivity, as a personality trait, exerts a modulatory influence over resting-state networks in TD children.
Jia et al., (2021)	TD children (n=54)	57.4 % (n=31)	11.59 ± 0.57	6’	Abacus-based Mental calculation (AMC)-trained children vs. Non-trained children	Cross-sectional	ReHo	Cuneus, Occipital middle, Temporal middle, (B) Frontal medial orbital, (B) Frontal medial, (L)Frontal medial inferior, (R)Frontal superior middle, (B)Cerebellum	Children trained in AMC show significantly better math skills and reasoning abilities, along with higher brain activity in the RPFC compared to those not trained. Specifically, the increased brain activity in the RPFC was linked to

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ID	Population (n)	% male	Age studied Range (mean, standard deviation)	Resting duration time	Comparison groups	Design	Analyses	Brain regions examined	Main findings
									better reasoning skills. These findings indicate that rs-fMRI might capture how training affects networks related to specific tasks.
Kim et al., (2015)	TD children (n=30)	73.3 % (n=22)	12.2 ±1.2	12'	Taekwondo trainers vs. Controls	Cross-sectional	ALFF	(R)Cerebellum, (B)MFG, (R)SFG, (L)Parietal lobe, (L)Precuneus, (L)Cuneus, (L) Lingual gyrus	Training in taekwondo enhances both physical agility and mental acuity by fostering stronger connections between the cerebellum and the frontal and parietal cortex of the brain.
Lee et al., (2023)	TD adolescents (n=128)	43 % (n=55)	9–14 1timepoint: (Boys: 11.81 ±0.87, Girls: 11.04±0.99) 2timepoint: (Boys: 13.83 ±0.90, Girls:13.09 ±1.06)	6'	Boys vs. Girls, 1 timepoint vs. 2 timepoint (2 years later)	Longitudinal, two waves	MVPA	(R)VLPFC, (R) PHG, (R)Lateral temporal cortex. (R)Insula cortex, (B)IPL, (R) VMPFC, (L)OFC, (L) Hippocampus, (B)Temporal pole, (L) Occipital cortex, (R)PCC	There are sex-dependent developmental trajectories regarding the DMN for externalizing and internalizing problems in adolescents. Internalizing problems are linked to the medial temporal subsystem for girls, and to dorsal medial subsystem for boys. Externalizing problems seem to be predicted by hyperconnectivity between DMN and FPN in boys, and hypoconnectivity between DMN and affective networks in girls.
Lei et al., (2014)	Healthy male adolescents (n=56)	100 % (n=56)	15.735±0.81	NR	High-activity MAOA genotype group vs. low-activity MAOA genotype group	Cross-sectional	ALFF	Pons	The MAOA gene regulates the association between impulsiveness and spontaneous activity in the pons for healthy male adolescents. Lower spontaneous brain activity in the pons of the MAOA-L male adolescents may be a neural mechanism by which boys with the MAOA-L genotype confers risk for impulsivity and aggression.
Li and Tian, (2014)	TD children and adolescents (n=134)	56.71 % (n=76)	Child group: 8.00–11.99 (10.22 ±1.11) Adolescent group:	8'	NA	Cross-sectional	ICA	FPN	The FPN plays a critical role in intelligence. Specifically, there is a relation between the FPN in

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ID	Population (n)	% male	Age studied Range (mean, standard deviation)	Resting duration time	Comparison groups	Design	Analyses	Brain regions examined	Main findings
			12.00–15.99 (13.47 ±0.81)						the (R) hemisphere during late-childhood, and in the (L) hemisphere during adolescence.
Li et al., (2019)	TD children (n=36)	47.2 % (n=19)	3–5(±0.16)	8'	3-years-old vs 5-years-old	Cross-sectional	ICA	(L)MTG, (B) MFG, (L) Precentral gyrus, (R)STG, (R) Caudate, (R) SFG, (L)IPL, (L) Lingual gyrus, (R)Cingulate gyrus, (R)Insula	Activation of the dorsal AN, DMN and bilateral FPN increases in 5-year-olds compared with 3-year-olds.
Li et al., (2020)	TD children (n=77)	45.45 % (n=35)	9–12 (10.17 ±0.95)	8'	NA	Cross-sectional	fALFF, seed-based analysis	(L)STG, (L)SMG, (R)PHG, Putamen	fALFF analysis indicates that increased aggression correlates with reduced activity in specific brain regions: the (L) temporal lobe, limbic area, and parietal lobe. These areas are closely involved in empathy and social cognition. Additionally, the rsFC analysis reveals a negative association between physical and overall aggressions and the FC between the (R) posterior hippocampal gyrus and the (R) putamen. This connectivity appears to moderate how neuroticism influences overall aggression levels.
Li et al., (2021)	Healthy adolescents (n=61)	95.08 % (n=58)	Combat sports group: 13–16 (14.2 ±1.1) Non-athlete control group: 13–16 (14.8±0.9)	8'	Combat sports group vs. Non-athlete control group	Cross-sectional	ICA	SMN, SMA, VN, DMN, IPL, MPFC, CEN, AN, SN, DACC, ECN, (B) DLPFC, AUN, PSTG	Compared with the controls, the combat sports group demonstrate increased intra-network FC within the SMN, VN and CEN. Besides, they show decreased inter-network FC was in the SMN-VN, SMN-AUN, SMN-DMN, AN-VN, and AN-ECN. The detected FC patterns in the combat sport group could be explained by neuromodulatory mechanisms, brain network improvements due to training,

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ID	Population (n)	% male	Age studied Range (mean, standard deviation)	Resting duration time	Comparison groups	Design	Analyses	Brain regions examined	Main findings
									potential early indications of minor brain injury, or inherent differences that existed previously.
Li et al., (2022)	Healthy adolescents (n=61)	95.08 % (n=58)	Combat sports group: 13–16 (14.2 ±1.1) Non-athlete control group: 13–16 (14.8±0.9)	8’	Combat sports group vs. Non-athlete control group	Cross-sectional	ALFF, ReHo, ICA	CEN	Combat sports affect cerebellar rs-fMRI (decreased intrinsic connectivity for ALFF and ReHo in the inferior CEN) and may cause compensatory functional changes (increased FC in the superior CEN).
Liang et al., (2022)	TD adolescents (n=109)	48.6 % (n=53)	8.2–14.6 (11.4±1.74)	7’ 12’’	Boys vs Girls	Cross-sectional	Seed-based analysis	(B)Posterior fusiform gyrus, (B)IOG, (L)ITG, (L)STG, (L) ventral IFG, (L) dorsal IFG	Girls show a stronger connection between visual orthographic areas and other regions of the reading neural network with age, while this trend is opposite for boys. Connections in boys that matter most for reading are lateralized, while in girls, connections between both sides were more crucial for reading ability.
Liu et al., (2019)	Healthy adolescents (n=216)	51.8 % (n=112)	(15.72 ± 0.94)	6’	NA	Cross-sectional	sDCM, ICA	VAN, VLPFC, TPJ	Effective connectivity between the (R) VLPFC and (L) TPJ within the VAN could potentially serve as a biomarker for self-reported depression in adolescents.
Liuzzi et al., (2023)	TD children (n=176)	48,9 % (n=86) 4 years old= 52,9 % (n=17) 6 years old= 65,5 % (n=18)	4–8 (6.27 ±1.49) Younger cohort 4 years old: (4.44±0.25) Older cohort 6 years old: (6.50±0.30)	7’ 6’’	Younger cohort vs. Older cohort	Longitudinal, two timepoints Cross-sectional	Seed-based analysis	(B)Amygdala, (B)Ventral striatum, MFG, Precentral gyrus, (B)PCC, PCG, (L) Caudate, (L) Lingual gyrus	Cross-sectionally, irritability is related to greater amygdala connectivity with PCC in early to middle childhood. Longitudinally, early childhood irritability may be linked to decreases in amygdala and ventral striatum connectivity with frontoparietal regions over time.
Manning et al., (2022)	TD children (n=35)	54.2 % (n=19)	3.25–3.75 (3.49±0.14)	8’	3-year-old children (1st timepoint) vs. 4-year-old children (2nd timepoint)	Longitudinal, two time points	ICA	(B)AG, Thalamus, Motor association cortex, (B) Fusiform, DLPFC, MPFC (R)MTG, (L)	Higher FC between frontoparietal language network, DMN and VN predict better pre-reading measures 1 year later.

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ID	Population (n)	% male	Age studied Range (mean, standard deviation)	Resting duration time	Comparison groups	Design	Analyses	Brain regions examined	Main findings
								Primary sensory cortex, (R) Somatosensory association cortex, (L) Anterior and DLPFC, (L) Broca's area pars opercularis, (L) DACC, (R)VACC, (L)SMG	Specifically, the superior longitudinal fasciculus and its connected cortical regions, along with the circuits linking the cerebellum and cerebral regions associated with reading, seem crucial for children's early reading skills.
Meijer et al., (2022a)	TD children (n=93)	53 % (n=49)	7.4–11.14 (9.2)	NR	Two intervention groups (aerobic exercise intervention or cognitively demanding exercise intervention) vs. Control group	Cross-sectional	ICA	VN, DMN, FPN, Somatomotor Network, DAN	14-week aerobic and cognitively demanding exercise interventions (in which the exposure to physical activity was doubled) are not sufficient to provoke changes in brain structure or functioning in children.
Meijer et al., (2022b)	Healthy children (n=90)	50 % (n=45)	8–11 (9.13 ±0.62)	NR	NA	Cross-sectional	Linear regression model	VN, DMN, FPN, Somatomotor Network, DAN	Brain activity in the FPN and the somatomotor network acts as a mediator between cardiovascular fitness and certain neurocognitive functions. Similarly, within the somatomotor network, brain activity also mediates the relation between gross motor skills and neurocognitive functioning.
Meri et al., (2023)	TD Children (n=29)	69 % (n=20)	8–12 (10 ±1.7)	5'	NA	Cross-sectional	Seed-based analysis	Fronto-parietal, Cingulo-opercular, VAN, DAN, CEN, SN	Screen exposure may reduce the engagement of basic attention and modulation of cognitive control networks and higher levels of parent-child interaction engage cognitive control networks.
Myers et al., (2016)	Healthy children (n=20)	55 % (n=11)	5.84–14.43 (9.32±2.12)	6'	NA	Cross-sectional	Whole-brain seed-to-voxel	(L)Caudate, (L) Thalamus, (L) AG, (L)Lateral occipital cortex, MPFC, Rostral ACC, DACC, (R) Frontal pole, DLPFC, PCC	Grit and growth mindset are both related to corticostriatal connectivity between ventral striatal cortex and DLPFC, which has been shown to be impaired in those with substance abuse and related to cognitive-behavioral control, more specifically,

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ID	Population (n)	% male	Age studied Range (mean, standard deviation)	Resting duration time	Comparison groups	Design	Analyses	Brain regions examined	Main findings
									inhibition, or the ability to ignore irrelevant or harmful stimuli.
Ruotsalainen et al., (2021)	TD adolescents (n=59)	34 % (n=20)	13–16 (14.3 ±0.9)	7' 5''	NA	Cross-sectional	ReHo, VMHC	SMG, Planum temporale, STG, Parietal operculum cortex, AG	In adolescents, more intense physical activity, but not aerobic fitness, is associated with higher levels of local FC in the brain.
Sánchez-Pérez et al., (2019)	TD children (n=56)	60.71 % (n=34)	Training group: 7–12 (9.06±1) Control group: 7–12 (9.22±1.31)	6'30''	Mathematical and working memory tasks training group vs. Control group	Longitudinal, two timepoints	Seed-based analysis	AN	Children undertaking mathematical and working memory program exhibit higher connectivity in attentional brain areas after training. This program also helps improve attention, non-verbal IQ, and mathematical and reading skills.
Sato et al., (2014)	TD children (n=447)	51.23 % (n=229)	7–15 (10.73 ±1.93)	NR	NA	Cross-sectional	Seed-based analysis	ECN, DACC, (L) IPL, VMPFC, (B) PCC, DMN, VMPFC, AMPFC, PCC, (B)PHG	The period between 7 and 15 is crucial for the development of the ECN and DMN, characterized by integration between posterior and anterior neuronal nodules and enhanced centrality in the hubs.
Sato et al., (2015)	TD children (n=447)	51.23 % (n=229)	7–15 (9.51 ±1.92)	6'	NA	Cross-sectional	Whole-brain graph analysis and data-driven	(L)AG, (L) Caudate nucleus, (R)Inferior semilunar lobe, (L)PHG, (R) Pyramis, (L) Cerebellar tonsils, (L) Cerebellum posterior lobe, (L)Caudate, (R) Fusiform gyrus, (R)Thalamus, (L) Parietal subgyral	During the transition from childhood to adolescence there is an increase in centrality and relevance of cortical areas with a decrease of subcortical and cerebellar regions. This suggests that hierarchical reorganization of the network over time is more important than changes in functional node-to-network integration.
Suñol et al., (2022)	Healthy children (n=227)	48 % (n=109)	8–12 (9.71 ±0.86)	6'	NA	Cross-sectional	Graph theory–based dynamic FC	(L)Ventral putamen, (L) Hippocampus, (L)Motor cortex, (B)SMA, (R) Superior parietal cortex	In healthy children, the changes in dynamic FC linked to obsessive-compulsive symptoms seem to align with brain circuits outlined by existing neurobiological

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ID	Population (n)	% male	Age studied Range (mean, standard deviation)	Resting duration time	Comparison groups	Design	Analyses	Brain regions examined	Main findings
									models of Obsessive-Compulsive Disorder. Additionally, there is further evidence suggesting the role of glutamatergic neurotransmission in these alterations within brain networks.
Swartz et al., (2021)	Healthy adolescents (n=70)	51.42 % (n=36)	12–15 (13.60 ±1.02)	6.7′	NA	Cross-sectional	Seed-to-voxel analysis	(B)Amygdala, (B)Accumbens, (B)Insula, MPFC, (B)IFG, (B)MFG	Peripheral inflammation seems to have unique associations in the adolescent brain, where resting-state connectivity plays an important role in the influence of inflammation on brain connectivity during adolescence.
Thieba et al., (2019)	TD children (n=44)	59 % (n=26)	3.5–6.3 (4.8 ±0.65)	8'20''	Monolingual vs Multilingual	Cross-sectional	Seed-based analysis	(B)SPL, (L)ITG, (L) MTG, (L) MFG, Anterior cingulate gyrus, (L) IPL	Compared to monolingual children, young children growing up in a multilingual environment have a more integrated functional language network that is less functionally connected to parts of the DMN and VAN.
Thomason et al., (2013)	TD children (n=33)	36.36 % (n=12)	7–15 (11.1 ±2.4)	6'	NA	Cross-sectional	Seed-based analysis	DMN	This study demonstrates for the first time that FC of the hippocampus is altered with changing cortisol levels: cortisol levels associate with hippocampal to DMN connectivity at rest in youth.
Wang and Huang, (2021)	TD children (n=10)	50 % (n=5)	10	8'	NA	Cross-sectional	ReHo	(L)DLPFC, (L) Frontal medial gyrus, (B) Posterior central gyrus, (B)PCC, (L) Middlepermall gyrus, (R) Supratemporal gyrus, (L) Inferioroccipital gyrus, Lingual gyrus	Short-term moderate-intensity aerobic exercise can improve brain plasticity and executive function by increasing local consistency of brain function in children at rest.
Wang et al., (2017)	Healthy adolescents (n=228)	47.81 % (n=109)	16.76–20.44 (18.48 ±0.55)	NR	NA	Cross-sectional	fALFF, seed-basedanalysis	DACC, DLPFC	At the regional level, there is an association between higher delay-discounting

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ID	Population (n)	% male	Age studied Range (mean, standard deviation)	Resting duration time	Comparison groups	Design	Analyses	Brain regions examined	Main findings
									and greater fALFF in the DACC. At the connectivity level, delay-discounting is positively correlated with the rs-FC between the DACC and the (L) DLPFC. Also, fALFF in the DACC and DACC-DLPFC connectivity uniquely predicts individual differences in delay-discounting.
Whitfield-Gabrieli et al., (2020)	Healthy children (n=94)	56.38 % (n=53)	07-nov	5.9′	7 years old (1st timepoint) vs. 11 years old (2nd timepoint)	4 year-longitudinal, two timepoints	ICA, seed-based analysis	MPFC, DLPFC, Subgenual ACC	Weaker connectivity between MPFC and DLPFC predicts improved attention, and weaker connectivity between subgenual ACC and DLPFC predicts worsening of internalization symptoms. Hence, these might be biomarkers during childhood that foster psychological alterations.
Winters and Hyde, (2022)	TD adolescents (n=122)	57 % (n=70)	13–17 (14.52 ±1.31)	10’	NA	Cross-sectional	NR	DMN, FPN, SN	Although callous unemotional trait and empathy seem to have similar neural correlates, the variance explained by each construct appears to be independent.
Winters et al., (2022)	Healthy adolescents (n=84)	NR	13–17	10’	NA	Cross-sectional	Seed-based analysis	DMN, MPFC, (B) AG, PCC, SN, ACC, (B)AI, (B) RPFC, FPN, (B) LPFC, (B)PPC	Neural correlates of empathy are moderated by the presence of callous unemotional traits in adolescents. Specifically, the association DMN-FPN seems to be a key element for understanding how callous unemotional traits change the relation between brain connectivity and affective empathy during adolescence.
Winters, Pruitt, et al., (2021)	TD adolescents (n=84)	53.6 % (n=45)	13–17	10’	NA	Cross-sectional	Seed-based analysis	DMN, MPFC, (B) AG, PCC, SN, ACC, (B)AI, (B) RPFC, FPN, (B) LPFC, (B)PPC	In adolescents, stronger connectivity within the DMN seems crucial for cognitive empathy. Also, the FC pattern of cognitive empathy

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ID	Population (n)	% male	Age studied Range (mean, standard deviation)	Resting duration time	Comparison groups	Design	Analyses	Brain regions examined	Main findings
									differs from that of affective empathy.
Winters, Sakai, et al., (2021)	TD adolescents (n=84)	55 % (n=46)	13–17	10'	NA	Cross-sectional	GIMME	DMN, MPFC, PCC, SN, ACC, (B)AI, FPN, (B) LPFC, (B)PPC	Callous Unemotional traits in adolescents are characterized by low density within the FPN and high density between DMN-FPN.
Xiao, Brauer, et al., (2016)	TD children (n=30)	50 % (n=15)	3-year-old group: (3 ±0.16) 5-year-old group: (5 ±0.16)	8'	3-year-old group vs. 5-year-old group	Cross-sectional	Seed-based analysis	(B)ASTG, (L) PSTG, (L)IFG	As a result of this study, it was found that there was an increase in left lateralization in the rs-FC of both the (L) PSTG and (L) IFG between the ages of 3 and 5 years. In the period from 3 to 5 years old, there is an increase of left lateralization in rs-FC of PSTG and IFG: IFG shows a leftward lateralization in 3-years-old and PSTG describes a rightward lateralization in 5-years-old. Therefore, LN experiences a developmental trajectory marked by age-dependency, increased long-range connections and dynamic hemispheric lateralization with age.
Xiao, Friederici, et al., (2016)	TD children (n=53)	50.9 % (n=27)	5–6 (5.5) 6–7.1 (6.5)	NR	5 years-old (time point 1) vs. 6 years-old (time point 2)	Longitudinal, two timepoints	DC, seed-based analysis	IFG, Inferior frontal sulcus, PCC, Precuneus, VMPFC, ACC	Increases in the (L) PSTG/STS are identified as significant changes in DC during a one-year period from 5 to 6 years old children. Connectivity of (L) PSTG/STS to language-relevant regions in (B) IFC is associated with greater advancement in language abilities, whereas connectivity of (L) PSTG/STS to DMN is linked to poorer advancement. This implies that connections within the LN notably evolve between ages 5 and 6 and significantly

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ID	Population (n)	% male	Age studied Range (mean, standard deviation)	Resting duration time	Comparison groups	Design	Analyses	Brain regions examined	Main findings
									impact behavior related to language development.
Xiao, Zhai, et al., (2016)	TD children (n=36)	47.2 % (n=19)	3–5(±0.16)	8'	3-years-old vs 5-years-old	Cross-sectional	Seed-based analysis	AMPFC, PCC, DMPFC, TPJ, Lateral temporal cortex, VMPFC, Posterior IPL, Retrosplenial cortex, PHC, Hippocampal formation	DMN undergoes a strong development from 3- to 5-year-old, and significant changes occur specifically in the medial temporal lobe subsystem. DMN is defined by stronger (R) hemispheric lateralization at age 3 but increasing (B) development through to age 5.
Xie et al., (2019)	Healthy early pubertal girls (n=84)	NA	HPG+ group: 8–11 (9.13 ±0.57) HPG- group: 8–11(8.92 ±0.37)	NR	Hypothalamus-pituitary-gonadal (HPG) positive group (HPG+) vs. Hyptothalamus-pituiraty-gonadal (HPG) negative group (HPG-)	Cross-sectional	ALFF	(B)STG	These findings suggested that the reactivated HPG axis and elevated prolactin level may affect brain activity and this effect may be the neuroendocrine basis of mood, cognition, and social behavior changes in early pubertal girls.
Xu et al., (2021)	TD children and adolescents (n=222)	59.9 % (n=133)	8–18 (12.35 ±2.6)	NR	NA	Cross-sectional	Seed-based analysis	Ventral striatum, DLPFC, Amygdala	There is neural evidence of the existence of the tradic model in adolescence, suggesting that reward sensitivity and risk avoidance reduce with age and evidence protracted cognitive maturation.
Yang et al., (2015)	TD children and adolescents (n=68)	55,55 % (n=40)	7.13–16.84 (12.13 ±2.74)	6'	NA	Cross-sectional	ReHo, fALFF, DC, VMHC, MDMR	(R)Lateral/ Medial visual area, Frontal gyrus, (B) Precuneus, (R) Pre- and postcentral gyrus, SPL, (L) Postcentral gyrus, (L)SFG, Cerebellum, (L) TPJ, (B)Lateral occipital cortex	Digital span forward performance shows more robust-age related differences in brain-behavior association than digital span backward. Also, it implicates a wider range of networks (VAN, DMN, Somatomotor Network, and Limbic Networks).
Yi et al., (2023)	Healthy children (n=69)	46.3 % (n=32)	9–12 (10.12 ±0.9)	8'	NA	Cross-sectional	Seed-based analysis	DMN, FPN, SN, Cingulo opercular network, VAN, DAN, Somatosensory motor-hand network, Somatosensory motor-mouth	Conscientiousness is associated to rs-FC between FPN and the somatosensory motor-hand network, and the AUN. FPN may play a key role in the neural

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Table 1 (*continued*)

ID	Population (n)	% male	Age studied Range (mean, standard deviation)	Resting duration time	Comparison groups	Design	Analyses	Brain regions examined	Main findings
								network, Subcortical network, VN, AUN, Memory retrieval network, CEN	performance of personality trait conscientiousness in children.
Yoon et al., (2022)	TD adolescents (n=70)	51.4 % (n=36)	12–15 (13.64)	NR	NA	Cross-sectional	Seed-based analysis	Amygdala, (L) Postcentral gyrus, (L)MTG, (R)Temporal pole	Amygdala connectivity patterns underlying extraversion in adolescents seem to be sex dependent. In girls, the amygdala's connections with the postcentral gyrus, MTG, and temporal pole are positively linked to extraversion. Conversely, boys show a negative connection.
Zhang et al., (2021)	TD children (n=64)	59.38 % (n=38)	Abacus-based mental calculation (AMC) training: 10.77–13.44 (11.93 ±0.51) Control group: 10.95–12.95 (11.95 ±0.49)	6'	Children with AMC training vs. Children without AMC training	Cross-sectional	fALFF	(R)MFG, (B)SFG, (L)Inferior occipital gyrus, (L)Middle occipital gyrus, (L)Fusiform, PCC, Precuneus, MCC, (L)SMA	The intrinsic community structure could get reconfigured toward more localized processing and segregated architecture after long-term cognitive training.
Zhang et al., (2023)	TD adolescents (n=231)	48 % (n=110)	16–20 (18.48 ±0.54)	NR	NA	Cross-sectional	fALFF, SEM	OFC	Trait emotional intelligence has a predictive role in depression and anxiety symptomatology in late adolescence. OFC connectivity may have a key role in the development of this trait in late adolescence.

Abbreviations. NR = not reported; NA = not applicable;(L) = left; (R) = right; (B) = bilateral; FC = functional connectivity; rs-FC = resting-state functional connectivity; TD = typically developing; ICA = independent component analysis; ALFF = amplitude of low-frequency fluctuations; fALFF = fractional amplitude of low-frequency fluctuations; SEM = structural equation model; DC = degree centrality; VMHC = voxel mirror homotopic connectivity; MDMR = multivariate distance matrix regression; ReHo = regional homogeneity; MVPA = multivoxel pattern analysis; sDCM = stochastic dynamic causal modeling; GIMME = group iterative multiple model estimation; IFG = inferior frontal gyrus; ITG = inferior temporal gyrus; dFC = dynamic functional connectivity; IFG = inferior frontal gyrus; MFG = middle frontal gyrus; SFG = superior frontal gyrus; ITG = inferior temporal gyrus; MTG = middle temporal gyrus; STS = superior temporal sulcus; SFG = superior frontal gyrus; VLFG = ventrolateral frontal gyrus; DLFG = dorsolateral frontal gyrus; ASTG = anterior superior temporal gyrus; PSTG = posterior superior temporal gyrus; MTL = medial temporal lobe; SMG = supramarginal gyrus; PHG = parahippocampal gyrus; IPL = inferior parietal lobe; LPFC = lateral prefrontal cortex; RPFC = rostral prefrontal cortex; MPFC = middle prefrontal cortex; VMPFC = ventromedial prefrontal cortex; AMPFC = anterior medial prefrontal cortex; VLPFC = ventrolateral prefrontal cortex; DMPFC = dorsomedial prefrontal cortex; DLPFC = dorsolateral prefrontal cortex; SPL = superior parietal lobe; MCC = middle cingulate cortex; AMCC = anterior middle cingulate cortex; ACC = anterior cingulate cortex; DACC = dorsal anterior cingulate cortex; VACC = ventral anterior cingulate cortex; PCC = posterior cingulate cortex; PCG = posterior cingulate gyrus; SMA = supplementary motor area; IOG = inferior occipital gyrus; TPJ = temporoparietal junction; IFG = inferior frontal gyrus; IFC = inferior frontal cortex; OFC = orbitofrontal cortex; AG = angular gyrus; AI = anterior insula; PPC = posterior parietal cortex; DMN = default mode network; SMN = sensorimotornetwork; VN = visual network; AUN = auditory network; AN = attention network; DAN = dorsal attention network; VAN = ventral attention network; ECN = executive control network; SN = salience network; LN = language network; CEN = cerebellar network; FPN = frontoparietal network connectivity within the Frontoparietal Language Network (FPLN) and phonological processing outcomes (Manning et al., 2022). Attentional processes in late childhood reveal associations between frontal areas and attentional performance (Whitfield-Gabrieli et al., 2020; Sánchez-Pérez et al., 2019), while reasoning abilities, studied through specific training such as abacus-based mental calculation, highlight adaptations in brain modular organization and correlations with prefrontal cortex activity (Zhang et al., 2021; Jia et al., 2021). However, the literature in early adolescence and specific cognitive domains remains sparse, with Liang et al. (2022) addressing sex differences in reading as a notable exception. Insights into late adolescence emphasize the role of motivation and reward processing, where delay-discounting behavior correlates with connectivity patterns in the dorsal anterior cingulate cortex (DACC) and dorsolateral prefrontal cortex (DLPFC) (Wang et al., 2017). This review underscores the importance of rs-FC studies in elucidating the neurodevelopmental pathways of diverse cognitive domains across youth.

Two thematic groups emerge from the sample of studies, each shedding light on crucial aspects of neurodevelopment. The first group, comprising Manning et al. (2022) and Xiao, Friederici, et al. (2016), delves into the intricate relation between early neurobiological development and language skills. Both studies utilize anatomical and functional imaging techniques, emphasizing the co-development of functional networks and brain structures in the early stages of childhood. The second group, encompassing Chahal et al. (2021); Liuzzi et al. (2023); Sánchez-Pérez et al. (2019); Whitfield-Gabrieli et al. (2020), focuses on the application of rs-fMRI to unravel behavioural and connectivity changes. These studies explore irritability's neural correlates, the role of ECN coherence in resilience, and the effectiveness of cognitive training programs, underscoring the intricate interplay between brain function and behaviour. Lastly, Agcaoglu et al. (2022) introduces a novel approach to longitudinal studies, utilizing a non-binning method for tracking spectral power changes in rs-fMRI data, providing detailed insights into typical brain development across different frequencies. Together, these studies contribute multifaceted perspectives to our understanding of neurodevelopment in children.

Understanding emotional regulation in childhood and adolescence is crucial for comprehending its neural foundations. Liuzzi et al. (2023) reveal the link between early childhood irritability and altered neural connectivity, predicting long-term changes. Correia et al. (2019) show how sensorimotor systems influence emotion perception. DeWitt et al. (2014) highlight hyperconnectivity in emotion regulation circuits during adolescence. Lee et al. (2023) uncovers sex-specific differences in neural architecture related to psychopathology. Together, these studies emphasize unravelling neural substrates for targeted interventions. Additionally, understanding emotional regulation changes over time can aid in early detection and treatment of disorders (Cullen et al., 2014; Malhi et al., 2019; Weise et al., 2020).

Personality traits, particularly impulsivity and risk-taking, were extensively examined across the reviewed studies. Hyperactivation within regions of the DMN was consistently associated with these traits (DeWitt et al., 2014; Inuggi et al., 2014). Li et al. (2020) identified hypoactivity in specific brain regions—left STG, right PHG, and left SMG—as correlating with aggressiveness in children. Moreover, Lei et al. (2014) highlighted the regulatory role of the MAOA gene in modulating impulsivity, particularly observed in the pons among male adolescents. Empathy, explored through the lens of callous-unemotional (CU) traits, revealed distinct neural signatures: while cognitive empathy was associated with increased DMN activity and hyperconnectivity between DMN and SN (Winters and Hyde, 2022; Winters, Pruitt et al., 2021), CU traits were linked to decreased DMN activity (Winters and Hyde, 2022). These findings underscore the intricate neural mechanisms underlying personality traits and emphasize their relevance in understanding socioemotional development during adolescence.

The brain areas and networks, DMN emerges prominently in our reviewed studies, playing critical roles across various developmental stages. Significant developmental enhancements in DMN connectivity, particularly between its anterior and posterior nodes, occur from early childhood to adolescence (Li et al., 2019; Sato et al., 2014; Xiao, Zhai et al., 2016). This network is implicated not only in typical cognitive development but also in conditions like impulsivity and empathy traits (DeWitt et al., 2014; Winters et al., 2022; Winters and Hyde, 2022). Conversely, the AN shows associations with subclinical depressive symptoms and is influenced by cognitive training and screen exposure during adolescence (Liu et al., 2019; Meri et al., 2023; Sánchez-Pérez et al., 2019). The FPN is integral to conscientiousness and intelligence development (Li and Tian, 2014; Yi et al., 2023), while the SN plays a crucial role in anxiety traits, showing hypoconnectivity patterns (DeSerisy et al., 2020; Geng et al., 2015).

Additionally, the VN exhibits sex-specific activity patterns related to reading skills and is influenced by activities like combat sports (Kim et al., 2015; Liang et al., 2022). The ECN emerges as a protective factor against internalizing symptoms during adolescence, particularly in more advanced stages of puberty (Chahal et al., 2021). Meanwhile, the SMN shows enhancements in connectivity due to physical activity and cognitive training interventions (Li et al., 2021; Zhang et al., 2021). Specific brain regions such as the amygdala and hippocampus are also pivotal, implicated in risk-taking behaviors, emotional regulation, and stress response modulation across developmental stages (Alarcón et al., 2015; Blankenship et al., 2017; Ge et al., 2021; Thomason et al., 2013).

Hemispheric asymmetry analysis illuminates brain functional organization in early development. Studies (Alcauter et al., 2017; Liang et al., 2022; Xiao, Brauer et al., 2016) reveal leftward lateralization in language networks during childhood and early adolescence. Key regions like prefrontal and superior temporal cortices drive language and reading skills in TD children. Initial bilateralization in 3-year-olds, rs-FC of PSTG was mainly bilateralized and rs-FC of IFG showed left lateralization. Both rs-FC of IFG and PSTG showed increasing left lateralization with age, but PSTG described a remaining dominance in rightward asymmetry at 5 years old (Xiao, Brauer et al., 2016). This extends previous findings about left lateralized intrinsic connectivity in language and reading throughout typical early development (Benischek et al., 2020; Reynolds et al., 2019). Liang et al. (2022) identify sex differences in brain lateralization: in boys, brain activity responsible for reading appears to be more left lateralized, whereas girls show less asymmetry and more inter-hemispheric connectivity. This finding is aligned with previous research that state sex differences in brain lateralization for reading (Bitan et al., 2010; Kumpulainen et al., 2023) and, also, some studies point that the sex differences in lateralization is an age-dependent effect (Hirnstein et al., 2013). On the contrary, the DMN exhibits a decreasing right dominance and increasing bilateral trend from 3 to 5 years old (Xiao, Zhai et al., 2016). While brain organization and lateralization of language and reading throughout the healthy youth is well-studied, lateralization trajectories of other cognitive domains remain unexplored.

Detecting biomarkers for healthy or impaired cognitive status has become a central goal of neuroimaging to drive health sciences towards precision. In this review, we identify some studies that are able to predict the evolution of mood symptoms. Decreased connectivity between frontal and posterior regions serves as a potential biomarker of internalizing symptoms in healthy adolescents. Liu et al. (2019) point to the connection between the right VLPFC and the left TPJ and, similarly, Whitfield-Gabrieli et al. (2020) claim that reduced subgenual ACC-DLPFC predicts a worsening of these symptoms in children. Stronger subgenual ACC-left DLPFC anticorrelations at this young age may indicate an attenuation or failure of top-down control mechanisms that appear later on adults with depression. Among late adolescents, weak fALFF in the OFC has a predictive role of diminishing the levels of depressive and anxiety symptoms in a sample of TD individuals (Zhang et al., 2023). Nonetheless, this systematic review does not allow us to conclude anything about the presence of biomarkers in children and adolescents and, therefore, we can only mention some studies included in this review that suggest the possibility of interpreting their results as the existence of potential biomarkers of mood symptoms.

Future directions may involve embracing a longitudinal approach to trace the developmental trajectory of neural networks from childhood through adolescence, elucidating the intricate interplay of age and sex. A crucial avenue for exploration is the impact of puberty and hormonal fluctuations on neural complexity, shedding light on the nuanced interplay between sex hormones and brain development during adolescence. Additionally, researchers might extend their analyses to investigate sex-specific patterns in functional network connectivity, unravelling how different brain regions communicate and synchronize during cognitive tasks or at rest. It would be valuable to examine the intricate relation between neural complexity and cognitive or behavioural outcomes, potentially paving the way for insights into educational and clinical interventions. Advanced machine learning techniques may prove instrumental in identifying subtle patterns within the data, facilitating the detection of sex-specific features and the development of predictive models for individual differences in neural complexity. Finally, fostering interdisciplinary collaboration among experts in neuroscience, psychology, nutrition, and education could offer a holistic approach to studying sex differences, considering both biological and environmental factors and enhancing our collective understanding of healthy brain development.

This review has limitations due to methodological variations and a lack of comprehensive longitudinal studies, hindering the understanding of cognitive and neural development. However, its broad scope and focus on longitudinal studies are strengths, emphasizing the importance of understanding developmental trajectories. Additionally, it highlights the relevance of emotional symptoms in adolescents for early detection and intervention.

5. Conclusions

Overall, this review emphasizes the importance of rs-fMRI in understanding typical brain development in youth, covering aspects from neural connectivity to gender differences and emotional regulation. While identifying developmental milestones like strengthened connectivity around age five, gaps remain in lateralization trajectories and connectivity variations at specific periods. Gender-specific connectivity patterns are crucial, suggesting the need for longitudinal studies, consideration of puberty, and interdisciplinary collaborations for a comprehensive understanding of brain development in youth.

Funding statement

This study was funded by Ministry of Science, Innovation and Universities/Agencia Estatal de Investigación/10.13039/501100011033 and European Social Fund Plus (PRE2022–102574, Project CEX2021–001159-M-20–4), and the Agency for Management of University and Research Grants of the Catalan Government (2021SGR00366).

CRediT authorship contribution statement

Guàrdia-Olmos Joan: Supervision, Project administration, Funding acquisition, Conceptualization. **Erwin Rogelio Villuendas-González:** Supervision, Conceptualization. **Maribel Peró-Cebollero:** Supervision, Funding acquisition, Conceptualization. **Ceren Kaya:** Formal analysis, Data curation. **Mérida Galilea Tapia-Medina:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Raquel Cosío-Guirado:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

Data will be made available on request.

Acknowledgments

The authors would like to thank Ministry of Science, Innovation and Universities/Agencia Estatal de Investigación/10.13039/501100011033 and European Social Fund Plus (Grant: PRE2022–102574, Project: CEX2021–001159-M-20–4) for institutional support.

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