Review

Brain imaging findings in children and adolescents with mental disorders: A cross-sectional review

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Background: While brain imaging studies of juvenile patients has expanded in recent years to investigate the cerebral neurophysiologic correlates of psychiatric disorders, this research field remains scarce. The aim of the present review was to cluster the main mental disorders according to the differential brain location of the imaging findings recently reported in children and adolescents reports. A second objective was to describe the worldwide distribution and the main directions of the recent magnetic resonance imaging (MRI) and positron tomography (PET) studies in these patients.

Methods: A survey of 423 MRI and PET articles published between 2005 and 2008 was performed. A principal component analysis (PCA), then an activation likelihood estimate (ALE) meta-analysis, were applied on brain regional information retrieved from articles in order to cluster the various disorders with respect to the cerebral structures where alterations were reported. Furthermore, descriptive analysis characterized the literature production.

Results: Two hundred and seventy-four articles involving children and adolescent patients were analyzed. Both the PCA and ALE methods clustered, three groups of diagnosed psychiatric disorders, according to the brain structural and functional locations: one group of affective disorders characterized by abnormalities of the frontal-limbic regions; a group of mental disorders with “cognition deficits” mainly related to cortex abnormalities; and one psychomotor condition associated with abnormalities in the basal ganglia. The descriptive analysis indicates a focus on attention deficit hyperactivity disorders and autism spectrum disorders, a general steady rise in the number of annual reports, and lead of US research.

Conclusion: This cross-sectional review of child and adolescent mental disorders based on neuroimaging findings suggests overlaps of brain locations that allow to cluster the diagnosed disorders into three sets with respectively marked affective, cognitive, and psychomotor phenomenology. Furthermore, the brain imaging research effort was unequally distributed across disorders, and did not reflect their prevalence.

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1. Introduction

While the majority of mental disorders have onset during childhood or adolescence, brain imaging techniques have generally been applied in adult patients. Studies in adults suggest involvement of various neuroanatomical and/or functional regional deviations in mental disorders. Brain imaging reports in juvenile patients subsequently suggested that some regional brain changes are also present in children or adolescents at onset, or even before, onset of psychiatric conditions [23,24,79,86,95,98]. The observation that brain abnormalities might be present early in life has lead to an increasing development of neuroimaging studies in children and adolescents in recent years.

Consequently, several reviews and meta-analyses have aimed at summarising the main findings related to juvenile subjects [3,4,1,79,88,94,106,117,1]. However, these reviews have generally focused on only one disorder, thus, there is no outline of recent neuroimaging studies of child and adolescent psychiatric conditions, neither as regards the similarities or differences of brain imaging features across disorders, during childhood or adolescence, nor as regards the worldwide distribution and representativity of the research effort.
The aim of the present review was to determine, which regional brain abnormalities were reported for each mental disorder and to pool them on that basis. To this end, we analysed all neuroimaging reports related to child and adolescent psychiatric disorders published between 2005 and 2008, a period during which a large number of studies were produced (more than 400 articles). Brain imaging includes several techniques, which provide anatomical (with sMRI and DTI), functional (with fMRI and PET) and metabolic (with MRS) data. Two other techniques, magnetocencephalography and electroencephalography, which measure the electric variations of the brain were not included in the present analysis because their spatial resolution is lower than MRI. As the present review was focussed on describing the locations of findings, but not their pathophysiology, we pooled the observations from all studies whatever the technique used by cerebral region and by disorder. Then, by means of PCA, and meta-analysis using the ALE method, we plotted the reported location of cerebral alterations and mental disorders, in search of overlaps.

A second objective was to provide the worldwide distribution and the main directions of these recent neuroimaging reports. Indeed, among the previous reviews, none has reported the geographical distribution of investigations, so the respective contribution of European, American, Asian, or other teams is unknown. Because brain imaging mental disorders in juveniles is a relatively new field, it is worthwhile assessing the contribution of each country in order to determine if the neuroimaging findings arise from homogeneously distributed regions. A further lack of information concerns the identification of the DSM IV mental disorders investigated – are neuroimaging studies focused on a subset of disorders or are all disorders investigated equally? – and the respective contribution of the various imaging techniques. Therefore, we carried out a descriptive analysis to characterise these reports by extracting the following information from articles published between 2005 and 2008: geographical distribution, annual progression, nature of the mental disorders and imaging techniques.

2. Methods

Neuroimaging literature reports of mental disorders in children and adolescents were included if they met the following criteria:

(i) the patient sample met international criteria for a psychiatric disorder;
(ii) neuroimaging techniques were used;
(iii) children or adolescents were the focus of the report.

Four hundred and twenty-three articles were identified in Medline databases between January, 2005 and December 31, 2008, using combinations of three keywords from the summary belonging to each of the following fields:

(i) neuropsychiatric disorders or psychotropic drugs (addiction, affective disorder, anorexia nervosa, anxiety, attention deficit hyperactivity disorder, autism, bipolar disorder, craving, depression, depression, hyperkinetic disorder, mental retardation, mood disorder, obsessive compulsive disorder, phobia, posttraumatic stress disorder, schizophrenia, Tourette’s syndrome/ alcohol, antidepressant, antipsychotic, anxiolytic, cannabis, cocaine, ecstasy, fluoroxetine, inhalant induced disorder, marijuana, nicotine, smoking, and tobacco);
(ii) age (adolescents, child, and children);
(iii) neuroimaging techniques (MRI, magnetic resonance spectroscopy, neuroimaging, and PET).

In addition, we reviewed the references of selected articles to identify other possible articles that might have escaped PubMed\(^1\).

Of the total 423 articles, 149 were excluded for any of the following reasons. The article was a review or a meta-analysis, the study included subjects older of 21 years (however we did not reject studies with a longitudinal design including subjects from children to young adults), or was conducted on high risk subjects affiliated with patient probands. We also excluded all case or pilot studies. After exclusion, a total of 274 articles remained (References are on the supplementary material in the online version of this article).

The following information was retained for analysis from each article: geographic location of the research team, year of publication, neuroimaging technique used, nature of the psychiatric disorder, and regions where significant structural and/or functional and/or metabolic abnormalities were observed in patients compared to healthy subjects of same age. As we could not include all the variously reported brain regions for analysis, we considered a common terminology for cerebral areas, in order to lower the number of variables. The inspection of abstracts allowed to select a number of regions with a terminology appearing recurrently. Thus, the authors’ observations were gathered into the following brain regions: frontal lobe, cingulum, amygdala, hippocampus (hippocampus and parahippocampus), temporal lobe, parietal lobe, occipital lobe, thalamus, striatum, amygdalae, hippocampus (hippocampus and parahippocampus), and cerebellum. Imaging techniques were not individualised because our aim was not to elucidate if the disorder was structural or functional but only to summarise the regional distribution of the reported abnormalities whatever their nature. Thus, we compiled, by cerebral region and by disorder, the observations from all studies when they revealed that brain images were significantly different in between-group (patients versus controls) comparisons. This was performed for addiction, anorexia nervosa, anxiety disorders (generalised anxiety, obsessive-compulsive disorder and post-traumatic stress), attention deficit hyperactivity disorders, autism spectrum disorders, mood disorders (major depressive and bipolar disorders), schizophrenia and Tourette’s syndrome. Only the mental retardation was excluded from this analysis, first because of its heterogeneity and second because no detail was provided on the location of alteration associated with this condition.

In order to cluster the disorders according to the locations of brain regional alteration, we performed a PCA using the R software package [78]. This statistical clustering method allows plotting of the association between items (i.e. mental disorders) and variables (i.e. cerebral regions), with the aid of a procedure extracting the main factors (graph axes F1 and F2) that reduce the dimensionality of multivariate data while preserving most of the variance therein. The output from PCA analysis consisted of score plots, which provided an indication of the differentiation of the mental disorders in terms of similarities in abnormalities locations, and a correlation plot giving an indication of correlations between variables with respect to their proximity. The PCA was performed on normalised data. Indeed, as the number of data was not the same for all disorders, to avoid a bias related to this difference, all data were reduced to unit one before PCA analysis. Thus, for each disorder, all numbers were divided by the maximum value, ranging data from 0 to 1.

Hence, in order to assess the consistency of the ACP results, we used the ALE meta-analytic technique developed by Turkeltaub et al. [103] in the subset of articles expressing the brain findings in Talairach’s or MNI stereotaxic coordinates. This method combines the coordinates of foci maxima from multiple studies into an ALE map for the brain, revealing between-study consistencies that may not be immediately evident by simple visual comparison of individual reports. We individually screened all the articles for the
presence of Talairach or MNI coordinates. Only foci in the source articles reported as significant at $p < 0.05$ corrected or $p < 0.01$ uncorrected were included. The studies were tabulated into the groups corresponding to the ACP results. Specifically, we analyzed the coordinates of 966 foci elicited by 82 different studies.

Detailed description of the ALE method and the statistical approach employed can be found in Turkeltaub et al. [103] and in Laird et al. [56]. Before analysis, the coordinates from studies that used the MNI templates were transformed into Talairach coordinate space [99]. Afterwards, all the coordinates were imported into a Java-based version of ALE software (http://www.brainmap.org/ale) and analyzed with a fully automated procedure. A statistical threshold of $p < 0.05$ was used for the generated activation likelihood estimation map, with a minimum cluster size of 100 mm$^3$.

The Talairach space was divided into $2 \times 2 \times 2$ mm$^3$ voxels and a whole-brain ALE map created by modeling the foci as localization probability distributions centered at the given coordinates; the probability each voxel was located within a particular focus was calculated using a 3D Gaussian function of 12 mm full-width half-maximum, computing the ALE value as the union of these probabilities, and then assessing statistical significance using the threshold determined by a permutation test of randomly generated sets of foci.

3. Results

3.1. Distribution of cerebral structures according to mental disorders in children and adolescents

The percentages of observations reported in each cerebral region with respect to each disorder are reported in Table 1. Results of the PCA and ALE analyses performed to cluster the mental disorders in terms of similarities in locations are reported respectively in Fig. 1, and in Table 2 and Fig. 2.

3.1.1. Location of brain abnormalities according to mental disorders.

Major depressive disorder was mainly associated with reports of structural and functional abnormalities in the frontal lobe (26.7% of observations), the anterior cingulate cortex (26.7%) and in the striatum (20%). Similar locations were reported in the bipolar disorder investigations. Studies on bipolar disorder also revealed abnormalities in the ventral prefrontal cortex, cingulate cortex, amygdala and hippocampus, respectively in 23.8%, 19% and 14.3% of observations.

In children and adolescents with anxiety disorders, the regions with the greatest numbers of observations were the frontal cortex (29.7%) and the amygdala (18.9%). The separate analysis of obsessive-compulsive disorder (six articles) revealed abnormalities involving the frontal (27.7%) and parietal (22.2%) cortices, the striatum (16.6%) and the thalamus (16.6%).

Data from studies on Tourette's syndrome revealed that alterations mainly involved the striatum (33.3%), thalamus (27.8%), and frontal cortex (22.2%). These regions were also suggested by neuroimaging studies on attention deficit hyperactivity disorders, with observations localised in the frontal cortex (26.3%), striatum (20.4%), parietal (16.8%), and cingulate cortices (12.4%).

Finally, autism spectrum disorders, schizophrenia, anorexia nervosa, and addiction mainly involved cortex regions. Indeed, most reports pointed out that autism was associated with abnormalities in the frontal (22.8%), temporal (18.8%), and parietal (14.9%) cortices, as schizophrenia with in addition abnormalities in hippocampus.

3.1.2. Principal component analysis.

Fig. 1A illustrates the dispersion of variables (i.e., regions) on the two first factorial axes (F1 and F2). As the data are mean-centred and scaled to unit variance, the angles between variables and factors (axes) represent correlation coefficients.

3.1.2.1. Factors. The first two principal factors (F1 and F2) jointly accounted for 68.31% of the total variance. The F1 axis (or x-axis) strongly correlated with posterior cortex variables (occipital, parietal, and temporal regions) on one side and lesser with amygdala and striatum on the other side. Thus, the F1 axis might separate cortical and subcortical regions. The F2 axis (or y-axis) correlated, on the one hand, with fronto-limbic structures (ventral frontal and cingulate cortex, amygdala and hippocampus) and, on the other hand, with the thalamus and striatum and might separate the fronto-limbic regions and the thalamo-striatal structures. The dispersion of variables (i.e., regions) and items (i.e., mental disorders) according to these two factors allowed plotting three groups of cerebral regions and three groups of disorders.

3.1.2.2. Variables. The following regions were included as variables: amygdala, cerebellum, cingulate areas, frontal lobe, hippocampus/parahippocampus, occipital lobe, parietal lobe, striatum, temporal lobe, and thalamus. The correlation plots indicated that the two axes (F1 and F2) allowed for the identification of three clusters of regions positively correlated within a group. This means that in most cases, if the number of observations in one region for a disorder was important, the number of observations in other correlated regions was also important for this disorder. A first group composed of neocortical regions was localised to the left of the x-axis (occipital, parietal, and temporal cortices), a second group composed mainly of limbic regions (amygdala, cingulate cortex, and hippocampus) was localised at top right of the y-axis, and a third group, including the striatum and the thalamus, was localised at the bottom right of y-axis.

3.1.2.3. Items. The following disorders were included as items: addiction, anorexia nervosa, anxiety disorders, attention deficit hyperactivity disorders, autism spectrum disorders, bipolar disorder, major depressive disorder, schizophrenia, and Tourette's syndrome. The two main factors or axes allowed pooling the disorders into three groups as shown on the score plots (Fig. 1B). The position of a disorder in a given direction within the score plots can be related to the variables regions that lie in the same direction on the correlation plots. The top right of the plot gathered affective disorders (anxiety, major depressive, and bipolar disorders) that all include emotional dysregulation. This first group of disorders appeared associated with the subcortical and fronto-limbic regions. The second group of disorders gathered addiction, anorexia nervosa, attention deficit hyperactivity disorders, autism spectrum disorders, and schizophrenia. All these mental disorders involve some degree of deviation in cognitive functions. This group clustered on the x-axis, thus appearing related to (posterior) cortical regions. The third group included only Tourette's syndrome, isolated on the y-axis, which appeared to be related to the striatum and thalamus regions. Its distance from the y-intercept denoted its singularity.

3.1.3. ALE analysis.

Three analyses were performed according to the groups of disorders revealed by the ACP. The coordinates and ALE value for each of the local maxima, as well as the volume of the corresponding cluster, are reported in Table 2.
3.1.3.1. Affective disorders. The ALE meta-analysis was carried out on 16 articles (10 on anxiety disorders, four on bipolar disorder and two on major depressive disorder) (Fig. 2A). It revealed 12 clusters of significant likelihood for activation \( (p < 0.05) \) found in right amygdala, bilateral cingular cortex (Brodmann areas 24 and 32), bilateral prefrontal association cortex (Brodmann areas 47, 10, and 11), left hypothalamus and left caudate body.

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\(^a\) One article is missing in the “annual distribution” because referenced in PubMed on December 2008 but published on 2009.

\(^b\) Among the 274 studies, four were single photon emission computed tomography (SPECT) studies (two on mental retardation, one on anxiety disorders and one on attention deficit hyperactivity disorders).

3.1.3.2. Mental disorders with cognition deviations. Sixty-four studies were included in the meta-analysis (attention deficit hyperactivity disorders, 25; autism spectrum disorders, 17; addiction, 12; schizophrenia, eight; and anorexia nervosa, two) (Fig. 2B). ALE results based on cognition disorders revealed 23 clusters of significant likelihood for foci. We found significant likelihoods of foci notably in cortical regions, including areas in bilateral frontal (Brodmann areas 47, 10, 9, 8, 6, and 4), parietal (Brodmann areas 40
and 7) and temporal lobes (Brodmann areas 41, 22 and 13) and left occipital lingual gyrus (Brodmann area 18). Significant clusters were also found in regions of basal ganglia.

### Tourette's syndrome

We found only two articles with Talairach coordinates usable for the ALE analysis. They draw one cluster of significant likelihood for focus \( p < 0.05 \) localized in left putamen.

### Characteristics of neuroimaging studies of psychiatric disorders in children and adolescents

Information was gathered on the worldwide distribution and the main directions of these recent neuroimaging studies (Table 1).

#### Geographic distribution

Most studies published between 2005 and 2008 were conducted in the United States laboratories (61.3% of the 274 reported articles). US research teams were mainly located in the states of California, Maryland, Michigan, and New-York. Around 23.4% of the studies were from Europe, with United Kingdom in first position, Germany in second, and Spain in third position. The remaining 15.3% involved research primarily from China and Canada (for details, see Fig. 3 and the additional table found in the online version of this article).

#### Neuroimaging techniques

Among the various MR imaging approaches, sMRI was in first and represented 49.6% of studies. This method was mostly used to investigate mental retardation (78.9% of studies), schizophrenia (74.1%), autism spectrum disorders (62.3%), and bipolar disorder (57.1%). fMRI was the second most common method, with 36.6% of the studies. It was mainly used to investigate anxiety disorders (63.2% of studies), attention deficit hyperactivity disorders (60.6%), and addiction (60%).
The number of neuroimaging studies in children and adolescent psychiatry rose from 46 in 2005 to 84 in 2008. This two-fold progression involved all mental disorders, with exception of bipolar disorder, for which the number of articles was constant throughout this 4 years period.

There were two predominant research fields: 46.8% of neuroimaging studies focused on attention deficit hyperactivity disorders and on autism spectrum disorders. Attention deficit hyperactivity disorders research was shared between the US (43.3%), Europe (31.3%), and other countries (25.4%), notably China. The main imaging techniques were fMRI (60.6% of studies) and sMRI (27.3% of studies). Autism spectrum disorders was primarily investigated with sMRI (62.3% of studies) in US laboratories (59% of studies).

Bipolar disorder represented 10.2% of neuroimaging studies (all reports came from the US), with 57.7% for sMRI and 21.4% for fMRI. Schizophrenia represented 9.9% of studies, with 55.6% from the US and the remainder from Europe. Almost all reports were sMRI (74.1%). The DTI technique was also frequently used to investigate the structural abnormalities related to these two disorders (14.8% of schizophrenia studies and 10.7% of bipolar disorder studies).

Mental retardation was a condition less-frequently investigated (7.7% of studies), more studied in Europe (38.1%) than in other parts of the world, and mainly with sMRI (78.9%). In contrast, addiction (7.3% of studies) and anxiety disorders (7.3% of studies) disorders were primarily investigated in the US (90% and 80% of studies, respectively). Anxiety disorders reports included subjects with generalized anxiety, obsessive-compulsive disorder and post-traumatic stress disorder. Regarding addiction, despite inclusion of all drugs of abuse in our keyword Medline search, the few brain imaging studies we found in adolescents concerned alcohol (12 articles), cannabis (eight articles) and tobacco (four articles) dependences. Major depressive disorder was a less investigated condition (5.5% of studies) and all reports were from the USA.

Finally, scarce studies focused on the Tourette’s syndrome (3.6% of studies) and anorexia nervosa (1.8% of studies); for this last disorder, only five articles were found from European research teams.

4. Discussion

This review examined brain abnormalities reported in neuroimaging studies of children and adolescents. The main finding was that brain abnormalities locations distinguished three groups of psychiatric diagnoses, including affective disorders associated with frontal – limbic changes, mental disorders involving cognition deviations associated with cortex changes, and a psychomotor disorder associated with basal ganglia abnormalities.

4.1. Mental disorders and location of brain abnormalities

Three groups of disorders were clustered using the PCA method according to location of the observed regional alterations. A group of emotion disorders, including anxiety and mood disorders, involved structural and functional abnormalities in the frontal cortex and the limbic system (amygdala, cingulate cortex, and hippocampus). A group of “cognitive” deficits (autism spectrum disorders, schizophrenia, attention deficit hyperactivity disorders, and addiction) mainly involved cortex abnormalities. A motor disorder, Tourette’s syndrome, was associated with alterations in the basal ganglia (the thalamus and striatum).

These results were supported by the ALE meta-analysis since this method, combining the stereotactic coordinates of the reported maxima from multiple studies into an ALE map, revealed that consistencies in cerebral regions between-studies were the same than those of the PCA procedure for the three groups of mental disorders. Thus, the ALE analysis carried out on articles...
related to emotion disorders revealed clusters of significant likelihood for activation in amygdala, cingulate cortex (Brodmann areas 24 and 32), prefrontal cortex (Brodmann areas 47, 10 and 11), hypothalamus, and caudate; those on Tourette's syndrome isolated one cluster in striatum; and those involving psychiatric disorders with “cognitive deficits”, clusters mainly located in frontal, parietal, temporal, and occipital cortices.

Present results support the models of early distinct brain regional systems in mental disorders. Thus, anxiety disorders and major depressive disorder are characterised by emotional dysregulation and are considered to be associated with dysfunction of the frontal-limbic system, and comorbidity between both disorders is often observed [45,96]. Consistently, the results presented herein compile all reports over 4 years and cluster both disorders with abnormalities of the frontal cortex and limbic regions. Moreover, the present report supports the idea that most abnormalities found in adults are already present in juvenile subjects with anxiety disorders [39,49,54,67–70,114], major depressive disorder [9,14,15,32,50,51,59,64,83,87], and bipolar disorder [2,8,18,28,29,46,72,75,82]. In spite of the implied similarities, compilation of these results suggests that each of these disorders had its own pattern of cerebral implications. Thus, at variance with anxiety disorders, major depressive disorder also involved cingulum and striatum abnormalities as revealed, for instance, by Forbes et al. [27] in an fMRI study. Also, within anxiety disorders, the separate estimation of structures involved in obsessive compulsive disorder revealed an implication of the fronto-striatal network (for instance, [114]), supporting this disorder would be distinct from others anxiety disorders with an involvement of cerebral dysfunctions more similar to those in Tourette's syndrome (see below).

The present results are also in agreement with the involvement of the frontal-striatal-thalamo-cortical loop in Tourette's syndrome because this disorder is linked on the score plots to striatum and thalamus abnormalities. Indeed, there is mounting evidence that Tourette's syndrome is an inherited developmental alteration of synaptic neurotransmission within the cortical-striatal-thalamo-cortical loops that would contribute to the relative inability to control tic behaviours by releasing motor production from regulatory control of the basal ganglia [4,6,31,37,58,60,63].

Attention deficit hyperactivity disorders is also a disorder with a motor component, and evidence suggests that it is associated with a disruption of the fronto-striatal-thalamo-cortical loop [13,90], as recent structural analyses revealed abnormalities in basal ganglia nuclei [91,102,104,109,111,115]. However, on the score plots of the PCA graph, attention deficit hyperactivity disorders appears to be linked with cortical abnormalities. This finding might be explained by the fact that attention deficit hyperactivity disorders is also related to parietal cortex abnormalities, as pointed out in recent literature [17,86,92,109]. Such cortical dysfunction might be related to the attention deficits that characterise this disorder and might also contribute in motor aspects of attention deficit hyperactivity disorders impulsivity. Consistently, functional neuroimaging studies during various attention tasks have revealed a dysfunction of the fronto-parietal system [10,16,52,53,93,97,100,105,107].

Finally, the present review supports autism spectrum disorders and schizophrenia in juvenile subjects are associated with marked cortical dysfunctions in parietal and temporal cortices, consistently with recent studies in autism spectrum disorders [7,11,22,30,33,36,37,48,61,65,76,80,85,89,110,113] and in schizophrenia [5,12,25,38,40,44,55,62,71,74,81,108,112]. It might be objected that some authors did report temporal abnormalities [5,38,40,112], a less consistently finding in the early-onset schizophrenia literature, and the present results might be influenced by the integration of young adults in two of the studies [38,112]. However, temporal abnormalities were also found in children [5,40], and even in the longitudinal study of Greenstein et al. [38], they were reported during early adolescence, before adulthood. The preeminence of posterior cortex abnormalities in adolescent schizophrenia patients is compatible with the model by Gogtay et al. [34,35] and Thompson et al. [101] findings of impaired cortex maturation processes in adolescents with schizophrenia involving a dynamic wave of white matter growth and a back-to-front wave of cortex gray matter loss, both maturation processes that have been revealed to be altered in adolescents with schizophrenia, by these authors.

4.2. Characteristics of neuroimaging studies

The present review also pointed out that structural and functional MRI studies in child and adolescent psychiatry in the US outnumber their European counterparts. This may be linked to the recommendations of the NIMH to prevent mental disorders. NIMH has elaborated a strategic plan that notably supports research that improves the understanding of the development, structure, and function of neural circuits, with a focus on those most relevant to mental disorders. This plan emphasizes the detection of biomarkers, biological indicators of disease processes, including brain abnormalities allowing early detection of disorders and, in turn, early intervention [143], http://www.nimh.nih.gov/about/strategic-planning-reports/index.shtml. It includes a focused research effort to define the developmental trajectories of mental disorders through the investigation of links between brain development and behavioural development, to understand how
brain regions critical for mental disorders are associated with typical and atypical behavioural functioning.

Aside from the lead of US research, the results reveal a steady rise in the number of annual studies showing interest in brain imaging psychiatric disorders in children and adolescents. Such an increase might be explained one hand by the need to reduce biases related to disease chronicity, long term treatments, and addictions, that are often inherent to studies conducted in adults, and on the other hand by the need to identify early brain abnormalities that might predate the onset of disorders. Thus, the identification of these abnormalities might be an important element of the quest for vulnerability factors and of biomarkers.

Regarding diagnoses, autism spectrum disorders, and attention deficit hyperactivity disorders were the most investigated. It is likely that interest has largely focused on these mental disorders in recent years because of their severity and frequency [26,116]. Still, brain imaging research in children and adolescents does not reflect the prevalence of psychiatric conditions at that age, since anxiety disorders and affective disorders, addictions, and eating disorders, which are more frequent, are notably under-investigated, based on this criteria [20,116].

5. Limitations

The present review has some limitations. First, the small number of studies in disorders such as anorexia nervosa, major depressive disorder, and Tourette's syndrome. Second, some studies in the present analysis included young adults within their participants, leading to the possible inclusion of cerebral structures where abnormalities are not related to childhood. However, there are less than 10 such studies, so that most results correspond to structures identified in children or adolescents. Third, the analysis was conducted through 2005 to 2008. Thus, previous studies were not included and consequently, cerebral regions strongly investigated before 2005 have escaped the present report. For instance, the first imaging studies on autism spectrum disorders focused on the cerebellum [21,42,47,73,77]. Fourth, the literature review was performed in the Medline database; despite it includes most scientific journals, it is not fully exhaustive. We searched for extra references however when inspecting the bibliography of the articles. Fifthly, the present review plotted fMRI, sMRI, PET and SRM studies, thus no conclusion can be drawn as regards pathophysiology mechanisms. Sixthly, the ALE analysis was carried out only on the reports (82 over 274) expressing results normalized as 3D-stereotactic coordinates. Indeed, multiple studies in the literature did report their results only in anatomically determined regions-of-interest. However, despite exclusion of a large part of studies, our ALE results are broadly consistent with those of our qualitative ACP that included both studies with and without stereotactic coordinates. A final limit regards the difficulty to name the second group of disorders identified in the present study. Indeed, the term “cognition deviations” is ambiguous because cognitive impairments are found also in Tourette's syndrome and in affective disorders. However, we found no designation that might fit all the four disorders (schizophrenia, autism spectrum disorders, attention deficit hyperactivity disorders and addiction) without referring to features pertaining to the other groups. Although debatable, our point was based on the theoretical distinction linking cognitive biases to “hot”, or “cold” cognition. In the group 2, the cognitive deviations involve disorders with marked alteration on emotion-independent, or “cold”, cognitive tasks requiring non-emotional information processing, while in group 1, emotion-dependent, or ‘hot’ cognition alteration is more readily related or secondary to changes in emotional information processing [1,84].

6. Conclusion

This review of the 2005–2008 literature on brain imaging in children and adolescents with mental disorders clustered disorders according to the location of cerebral abnormalities. It supports the hypothesis that the clustered diagnoses include behaviour deviations that might share dimensions linked with common regional brain systems. The findings also point out the scarcity of studies on major depressive disorder, a common group of childhood disorders that tends to worsen if not treated early, and on anorexia nervosa.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.eurpsy.2010.04.010.

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