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Cognitive, Neurobiological and Psychopathological Alterations Associated with Child Maltreatment: A Review of Systematic Reviews

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Abstract The impact of childhood maltreatment has been studied in the last decades in several countries. This study aims to provide a review of systematic reviews about the relationship between neurobiological and cognitive impairments, psychiatric disorders and child maltreatment. PsycInfo, Pubmed and Scielo databases were searched to include reviews published from 2004 to 2014. Fifteen reviews about the impact of child maltreatment were analysed. Four of them deal with the neurobiological effects, two with the cognitive damages, and nine of them with the development of psychiatric disorders throughout the victim's lifetime. The association between childhood maltreatment and the development of psychiatric disorders is the one that has received the most attention in the last few decades. The impact of maltreatment in cognition, above all in childhood, has been the least studied area; few studies, presenting conflicting results, were found.

Keywords Child maltreatment · Abuse · Neglect

1 Introduction

According to the World Health Organization (WHO), approximately 20 % of women and 5–10 % of men report having suffered sexual abuse in childhood, and 23 % of adults report having been a victim of physical abuse as children (Butchart et al. 2006). Such situations, together with emotional abuse and negligence, are conceptualized as

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maltreatment and may generate several emotional and cognitive damages throughout life (Yehuda et al. 2001; Dannlowski et al. 2013). These kinds of maltreatment can be perpetuated in several contexts, such as within the family, in school, and others.

The World Health Organization (WHO) defines physical abuse as the intentional use of force against the child or adolescent, and includes behaviors such as, *inter alia*, hitting, kicking, burning, poisoning and suffocating the victim, often as a punishment, resulting in risk of death and in developmental and health issues. Sexual abuse, on the other hand, is defined as the contact of someone in a more advanced stage of psychosexual development with a child or adolescent, who is unable to fully understand or consent, with the objective of sexual stimulation (Habigzang et al. 2005; Krug et al. 2002). Psychological or emotional abuse can be defined as a failure of the parents or caregivers in providing an adequate environment for the development of the child or adolescent, and includes behaviors such as blaming, scaring, discriminating and humiliating the victim, among others. Negligence is characterized by the failure of the parents or caregivers in providing health, education, emotional development, nutrition and a safe space to live (Butchart et al. 2006; Hart and Rubia 2012; Krug et al. 2002).

Childhood is the most important part of life as far as a person's emotional and cognitive development is concerned. Even though it is now known that the brain undergoes structural and functional modifications until the third decade of life, 90 % of brain size is already developed by age five, and childhood is the primordial time for brain development and maturation (Lebel and Beaulieu 2011; Lenroot and Giedd 2006). Scientific literature shows that, for most victims, maltreatment is associated with important neurobiological changes reflected in both cognition and emotion. Children who suffered maltreatment present deficits particularly in executive functions, which impact their academic and social development in both short and long-term (Diamond 2012). Neurobiological sequelae in regions related to emotional regulation, such as a shrinkage in prefrontal and limbic structures, might favor the development of several psychiatric disorders throughout life (Huang 2014; Pechtel and Pizzagalli 2011). There is also a feedback loop between these two areas, since the consequences of cognitive malfunctions (e.g., academic failure and difficulties in social relationships) might increase the child's vulnerability to further emotional sequelae (Diamond 2012). Anxiety, depression and PTSD may also generate neurobiological sequelae and cognitive impairments, further strengthening this feedback loop (MacQueen and Frodl 2011; Hayes et al. 2011).

In the other hand, the high prevalence of child maltreatment has an impact on many more victims than those directly involved. Public policies for its prevention and treatment demand significant resources from society. An evaluation estimates that the United States spends US$ 33 billion per year in direct interventions, such as the hospitalization of child victims of physical abuse and familial interventions, and US$ 46 billion per year are indirectly spent with the educational needs and legal problems caused by the associated juvenile delinquency (Gelles and Perlman 2012). In the United Kingdom, an estimated £1.14 billion are spent yearly by social service programs related to this problem. However, even though we have direct cost estimates for several countries, it is impossible to determine an exact value for the financial impact caused by maltreatment as a whole, considering that resources are needed for both direct and indirect interventions in different areas of healthcare, law, and social programs. According to the WHO, these costs may, ultimately, delay a country's social and economic development (WHO 2014).

Scientific literature from the last few decades has described several damages associated with child maltreatment, including neurobiological and cognitive changes, as well as several psychiatric diagnoses strongly associated with such experiences. However, not much attention has been given to an integrated understanding of these findings (Pechtel and Pizzagalli 2011). The joint analysis of such alterations might generate hypotheses about the feedback mechanism involved in these sequelae. Therefore, the objective of this study is to present a review of systematic reviews about neurobiological and cognitive alterations and psychiatric disorders associated with child maltreatment, while discussing these impairments in an integrative fashion.

2 Method

The literature review has been conducted between December 2013 and January 2014 in the PsycInfo, Pubmed and Scielo databases. The structure of the study follow the PRISMA recommendations. All abstracts of systematic reviews and meta-analyses on child maltreatment in English, French, Spanish or Portuguese published between 2004 and 2014 were identified, totalizing 381 abstracts. The following exclusion criteria were then applied, excluding: (i) articles published in languages other than those mentioned; (ii) articles which were not systematic reviews or meta-analyses; (iii) articles which did not deal with child maltreatment; (iv) articles which did not deal with the neurobiological or cognitive damages and/or associated psychiatric disorders. The abstracts of the articles were analysed independently by the first three authors of this paper. Each author's findings were compared and, when disagreements occurred, another author decided the inclusion or exclusion of a study. This procedure left 66 articles, the full texts of which were analysed for elegibility by the authors, with the application of the same exclusion criteria, leaving 15 articles included. A schematic view of the selection process can be seen in Fig. 1.

3 Results

As seen in Table 1, fifteen articles about the impact of child maltreatment were analysed. Four of them dealt with the neurobiological effects, two with the cognitive damages, and nine of them with the evolution of psychiatric disorders throughout the victim's lifetime. The findings are described below according to the type of impact.

3.1 Neurobiological Effects

Diseth (2005) conducted a systematic review of publications from 1993 to 2003 in order to update the concept of dissociation related to traumatic experiences in children and adolescents, and also to present new perspectives on the related subcortical processes. Most of the articles on the traumatic correlates showed a strong association between persistent child abuse, particularly persistent sexual child abuse, and dissociative experiences in adult life. These articles indicate young age at the beginning of trauma and traumatic events' frequency as the factors which predispose towards dissociative symptoms. Despite the fact that most studies focus on sexual abuse,

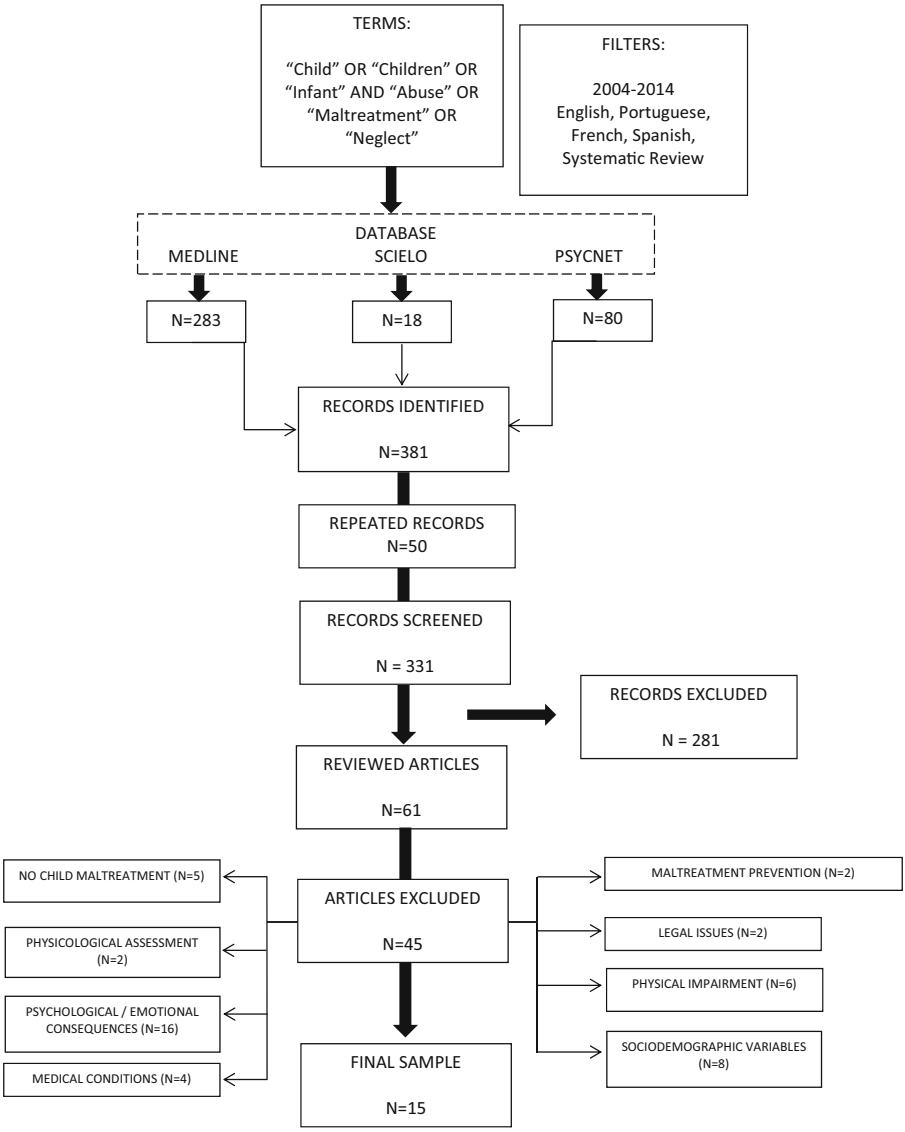

Fig. 1 Summary of search strategy and study selection

scientific literature has begun to direct its attention also to physical and psychological abuse and to negligence, finding that these kinds of maltreatment may also be linked to dissociative symptoms.

The articles on neurobiological correlates were classified into different groups as they dealt with neurochemical, functional or structural abnormalities, or dysfunctions in the development of the limbic and neocortical systems. The most significant neurochemical alterations were pathological responses in the Hypothalamic-Pituitary-Adrenal (HPA) axis. In the case of exposure to chronic stress, normal to low cortisol levels are found, caused by down-regulation in the hippocampus within the HPA axis,

Table 1 Summary of studies included and main results

Study	Type of Study	Database	Included articles/ Total of participants	Main Results
Neurobiological sequelae				
Diseth 2005	Systematic Review	PubMed and PsychInfo	932/NR	Significant association between recurring child maltreatment, especially sexual abuse, and dissociative experiences in adulthood.
Woon and Hedges 2008	Meta-analysis	PubMed and PsycInfo	8/396	Adults with PTSD associated with maltreatment presented reductions in the volumes of the right and left areas of the hippocampus compared to the control group, with a moderate effect size.
Pereda and Gallardo-Pujol 2011	Systematic Review	Medline, Scopus, Psycinfo and ISI Web of Science	34/1869	Studies with children and adults indicated neuroendocrine, neurostructural and neurofunctional changes associated with different types of abuse, especially sexual abuse.
Von Werne Baes et al. 2012	Systematic Review	PubMed, SCOPUS and Scielo	34/3265	Evidence of an important role of ELS in persistent neurobiological adaptations that make some individuals vulnerable to developing depression in adult life.
Cognitive sequelae				
Parks et al. 2007	Systematic Review	Psycinfo, MEDLINE, EMBASE, Social Science Citation Index, Science Citation Index, CINAHL, Biological Abstracts, ASSIA, INSPEC, HMIC/DH Data, British Nursing Index, SPORT Discus, AMED, Enconlit, Index to Theses and International Bibliography of the Social Sciences	10/2000	Child and adolescent victims of physical and sexual abuse had greater attentional impairment, higher levels of depression and greater risk of victimization than the group with victims of only one type of abuse.
Irigaray et al. 2013	Systematic Review	Medline, PsycInfo, Embase and Amed	17/1350	Adults and children who had suffered maltreatment presented a range of cognitive impairments, especially in declarative memory and executive functions.
Psychiatric sequelae				
Fry, McCoy & Swales 2012	Systematic Review	PubMed/Medline, ProQuest, PsycINFO, ScienceDirect,	106/NR	Children who suffered sexual abuse presented, on average, a twofold risk of developing a psychiatric disorder compared

Table 1 (continued)

Study	Type of Study	Database	Included articles/ Total of participants	Main Results
		CINAHL-ebsco, EMBASE, ERIC, NCJRS, Violence and Abuse Abstracts, Social Work Abstracts, SocIndex, Family and Society Studies Worldwide, Google, Google Scholar, SSCI e Korea Med		to children who did not suffer any kind of maltreatment. Similar results were found for other kinds of maltreatment, such as negligence, physical and sexual abuse and domestic violence during childhood.
Hillberg et al. 2011	Systematic Review	Campbell Collaboration, The Centre for Reviews and Dissemination, The Cochrane Library, Cumulative Index to Nursing and Allied Health Literature, Cambridge Scientific Abstracts, Applied Social Science Index and Abstracts, Education Resources Information Center, Social Services Abstracts, Sociological Abstracts, Embase, Medline Index, Medline Non-Index; Science Direct, Social Service Information Gateway, Swetswise, PsycINFO; Zetoc , and Web of Science	7/NR	Individuals who were sexually abused in childhood were at increased risk for the development of psychopathologies in adulthood, with greater effect size in the relationship between child sexual abuse and borderline personality disorder, PTSD, depression and anxiety symptoms
Hillberg et al. 2011	Systematic Review	Campbell Collaboration, The Centre for Reviews and Dissemination, The Cochrane Library, Cumulative Index to Nursing and Allied Health Literature, Cambridge Scientific Abstracts, Applied Social Science Index and Abstracts, Education Resources Information Center, Social Services Abstracts, Sociological Abstracts,	7/NR	Individuals who were sexually abused in childhood were at increased risk for the development of psychopathologies in adulthood, with greater effect size in the relationship between child sexual abuse and borderline personality disorder, PTSD, depression and anxiety symptoms

Table 1 (continued)

Study	Type of Study	Database	Included articles/ Total of participants	Main Results
		Embase, Medline Index, Medline Non-Index; Science Direct, Social Service Information Gateway, Swetswise, PsycINFO; Zetoc , and Web of Science		
Martins et al. 2011	Systematic Review	PubMed and Scielo	31/NR	Significant association between the presence of some type of stressor in childhood and psychiatric diagnosis in 94 % of the analyzed articles. The most frequent association was with anxiety disorders (including agoraphobia, panic disorder, social phobia, specific phobia and PTSD), followed by mood disorders and alcohol dependence.
Maniglio 2010	Systematic Review	AMED, Cochrane Reviews, EBSCO, ERIC,MEDLINE, PsycINFO, and ScienceDirect	4/60.000	Significant correlations between child sexual abuse and depression in adulthood were found. The magnitude of these associations ranged from small to median.
Maniglio 2011	Systematic Review	AMED, Cochrane Reviews, EBSCO, ERIC, MEDLINE, PsycINFO, and ScienceDirect	6/NR	A significant association between child sexual abuse and substance-related disorders was found. The magnitude of this association was small to median. An effect of gender was found in alcoholism, as it was strongly associated with women who had experienced sexual abuse in childhood.
Maniglio, 2013a	Systematic Review	AMED, Cochrane Reviews, EBSCO, ERIC, MEDLINE, PsycINFO and ScienceDirect	4/3.214.482	Significant association between childhood sexual abuse and anxiety symptoms, such as obsessive-compulsive, post-traumatic and phobic, with a small to medium magnitude. Some types of anxiety symptoms, such as phobic symptoms, were statistically less significant than others, such as post-traumatic symptoms.
Maniglio 2013b	Systematic Review	EBSCO, ERIC, MEDLINE (PubMed e PubMed Central), PsycINFO and Science Direct	20/3407	Individuals with bipolar disorder reported more childhood sexual abuse experiences than individuals without this psychopathology. However, when compared to individuals with other psychopathologies, such as depression

Table 1 (continued)

Study	Type of Study	Database	Included articles/ Total of participants	Main Results
				and schizophrenia, individuals with bipolar disorder tended to report lower or similar rates of childhood sexual abuse.
Norman et al. 2012	Systematic Review	Medline, EMBASE and PsycINFO	124/1.185.363	Significant association between non-sexual child abuse and depression and anxiety. Physical abuse correlates more closely with eating and conduct disorders, while emotional abuse and negligence are more associated with substance use disorders.

NR the article does not report the total number of participants

which leads to the suppression of the response to stress based on negative feedback or changes in the number of receptors. The low levels of cortisol may cause an important change in fear and fight/flight responses.

Some studies found abnormally elevated noradrenalin and dopamine secretion in traumatized children, as well as few platelet adrenergic receptors and an increase in cardiac frequency at rest, indicating a super activation of the sympathetic nervous system. These alterations generate responses interpreted as threats by the amygdala, resulting in a sympathetic response even when the child is not facing a real stressor. A significant association between higher parasympathetic system activation and dissociative responses was also found. The vagal nerve is activated by noradrenalin, causing decreases of the heart rate and blood pressure as well as the secretion of endorphins associated with the dopaminergic system in the prefrontal cortex. In a clinical context, Diseth (2005) hypothesized that, following this pattern, children may come to react to weaker stressors and thereby generate dissociative responses. Among functional changes, the EEG studies showed that, when participants who have undergone some trauma remember or are exposed to a traumatic memory, the two brain hemispheres present a marked hemispheric lateralization, with stronger brain activity in the right side; greater activation of emotion-related areas such as the amygdala, the right temporal cortex, the prefrontal cortex, and the right visual cortex. These alterations, together with a lower activation of the Broca area, suggest that emotions are experienced by dissociative patients as physical, visual and nonverbal memories; and abnormalities in the EEG of the left temporal and frontal regions. EEG coherence analyses indicate that the right hemisphere is significantly more developed than the left hemisphere in right-handed children who have been abused. Regarding structural abnormalities, it was found that the total volume of the brain and the corpus callosum were reduced, as well as other dysfunctions in the development of limbic structures, such as the amygdala and the hippocampus.

The meta-analysis of Woon and Hedges (2008) containing articles published between 1997 and 2007 revised data about hippocampal and amygdala volume in children and adults with maltreatment-related post-traumatic stress disorder (PTSD). No differences in hippocampal or amygdala volume, nor any asymmetry between the right and left sides of the brain were found between the children with or without PTSD. However, the volumes of the right and left hippocampi were found to be lower in PTSD-suffering adults in comparison with the control group, a result with a moderate effect (left effect size=−0.635; right effect size=−0.414). The adult control group presented asymmetric hippocampus, with the left side bigger than the right side, but maltreatment-related PTSD-suffering adults did not. The authors suggest that child maltreatment resulting in PTSD may interrupt the normal development of the hippocampus. The findings indicate that children keep their hippocampus "intact", but the reduction in hippocampal volume indicates that an atrophy may occur at some point between childhood and adolescence. A comparison between amygdala volume in children and adults with maltreatment-related PTSD was not conducted because the authors found just one article which examined amygdala volume in adults. They recognized that limitations such as the low number of studies dealing with the relationship between maltreatment and amygdala and hippocampal volume, what made it impossible to make a robust analysis controlling for variables such as gender, maltreatment duration, age, and gravity of the post-traumatic symptoms, and recommend that longitudinal studies should be conducted.

Pereda and Gallardo-Pujol (2011) present an update of findings on the main neurobiological alterations after sexual abuse in childhood. Their analysis included articles on child maltreatment and sexual abuse-related neuroendrocrine, structural, functional and neuropsychological abnormalities published between 1999 and 2010. One of the most important neuroendocrine alterations found is on the HPA axis, which shows elevated dopamine, noradrenalin, adrenalin and cortisol in subjects who suffered abuse in comparison with those who did not. The effect on cortisol is especially interesting because of its relationship with exposure to stress and the development of psychopathologies. The authors suggest that maltreatment experiences sensitize the HPA axis and the autonomous response to stress, thereby increasing the risk of psychiatric disorders.

Regarding structural changes, the studies show that maltreatment during childhood interferes in the development of the nervous system in general, as in the total brain volume, and in the specific development of the brain structure, particularly the size of the hippocampus and the volume of the lateral ventricles of the prefrontal cortex and the anterior cingulate cortex. The studies associate lower hippocampal volume to younger age at the start of the maltreatment as well as to lower hippocampal volume and to maltreatment duration. Other structural abnormalities include a reduction in the amygdala and the left hippocampus, in comparison with non-maltreated controls. These results are found in both children and adults who suffered maltreatment in childhood. Women who suffered sexual abuse also present reduced volume in the primary visual cortex and in the visual association cortex, both proportional to the duration of the abuse.

Functional alterations accompanying structural alterations include greater activation in the cerebellum, the left inferior frontal gyrus, and the thalamus, when the subjects are confronted with stories regarding the traumatic situations they experienced. A study with female victims of sexual abuse revealed an abnormal connectivity in several limbic structures, such as lower activation of dentate gyrus, and greater activation of the amygdala. These findings suggest the possibility of impairment in processes involving learning and conditioning, together with impairment in the process of fear extinction. This review highlights that few studies evaluated the different kinds of maltreatment, a limitation that makes it impossible to draw specific conclusions about sexual abuse and the differences between this and other kinds of abuse.

The systematic review of Baes, Tofoli, Martins, and Juruena, 2012 included publications dated from 2000 to 2011 dealing with the activity of glucocorticoid and mineralocorticoid receptors in the HPA axis, particularly in depressed patients with Early Life Stress (ELS). Various types of chronic and acute stressful events occurring in childhood were included in the broad ELS concept, such as abuse, neglect, parental loss and other psychosocial stressors. Out of the 34 evaluated papers, nine dealt with the activity of the HPA axis in individuals with ELS, six of which discussed the HPA axis in patients with depression-related ELS, and three in patients with ELS but no psychiatric disorders. Four of the studies utilized the *Childhood Trauma Questionnaire* (CTQ), three utilized the *Early Trauma Inventory* (ETI), two utilized the *Childhood Experiences of Care and Abuse Questionnaire* (CECA-Q and CECA) and one used the *Parental Bonding Instrument* (PBI).

Five of the nine studies mentioned used the *Dexamethasone/Corticotropin Releasing Hormone Test* (Dex/CRH) to evaluate the activity of the HPA axis and obtained dissimilar results. Three studies found lower plasmatic cortisol levels in

individuals who underwent ELS compared with controls, while two studies found higher cortisol levels. While the direction of the change is controversial, these studies agree that individuals who suffered ELS show alterations in the HPA axis. Two other studies evaluated HPA axis activity using the *Dexamethasone Suppression Test* (DST); one of them found no influence of ELS in HPA axis activity in depressed patients, while the other found lower cortisol and ACTH levels in women who suffered from depression and ELS. A further two studies evaluated HPA axis activity using the *Prednisolone Suppression Test* (PST), and neither found significant differences in cortisol suppression between depressed patients with and without ELS. The authors concluded that, despite dissimilar results, there is general evidence for an important role of ELS in persistent neurobiological adaptations which might make some individuals vulnerable to developing depression in adult life.

3.2 Cognitive Dysfunction

Parks et al. (2007) evaluated cognitive damages in homeless children and adolescents, however out of ten included articles, just one dealt specifically with maltreatment. This study was conducted with homeless adolescents who reported having suffered sexual and physical abuse in the past. The authors concluded that the adolescents who suffered both these kinds of abuse showed bigger attention deficits, higher rates of depression, stronger symptoms and higher revictimization risk when compared to other adolescents who underwent only one kind of abuse.

The review made by Irigaray et al. (2013) included articles published between 1995 and 2011 dealing with exposure to maltreatment in childhood and its effect on both short-term and long-term cognitive functioning. Eleven articles with adult samples and six with child samples were found. Sexual abuse was the most frequently studied kind of maltreatment and most of the total sample was composed by adult women. Of the six studies on children, four found larger deficits in cognitive functions such as working memory, problem solving, abstract reasoning, word naming, planning, inhibition, and mental flexibility, in visuospatial function, in visual-motor integration and in language. Seven of the eleven studies on the long-term effect of childhood maltreatment showed significant differences between the maltreated group and the control group, with deficits in declarative memory and executive functions such as problem solving, planning ahead, mental flexibility (set-shifting), the central executive component of working memory, inhibition, information processing speed and abstract reasoning. Maltreatment severity was linked to lower general intelligence quotients (IQ) and lower declarative verbal memory. Abuse duration was strongly linked to deficits in all kinds of memory. One linear regression, conducted by Navalta *et al*. (2006), indicates that short-term memory decreases by 2.4 %, verbal memory by 2.0 %, visual memory by 1.9 %, and global memory by 2.3 %, for each year of abuse. The authors of this review point out the heterogeneity of evaluation instruments and methods, the small number of the samples, the focus on adults, women, sexual and physical abuse as limitations of the studies they reviewed.

3.3 Psychiatric Disorders

Fry, McCoy and Swales (2012) conducted a systematic review of scientific articles and "grey literature" produced between 2000 and November 2010 dealing with the

consequences of childhood maltreatment in the Asia-Pacific region. One hundred and six studies were included. The results were divided into five categories: (1) consequences on mental health; (2) consequences on physical health; (3) consequences on sexual health; (4) consequences on intrafamilial violence; (5) other behaviors. Fifteen studies included in the review focused on maltreatment's consequences in mental health. Most studies used the Symptom Checklist-90 (SLC-90), an instrument that measures psychiatric symptoms in the last seven days, including symptoms such as somatization, obsessive-compulsive behaviors, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism. Children who suffered sexual abuse presented, on average, twice as much risk of developing a psychiatric disorder compared to children who did not suffer any kind of maltreatment. Similar results were found for other kinds of maltreatment, such as negligence, physical and sexual abuse, and domestic violence during childhood. Higher levels of depressive and dissociative symptoms, as well as suicide ideation, were also found in victims of childhood maltreatment.

Maniglio (2010) reviewed articles published between 1966 and 2008 on the relationship between childhood sexual abuse and depression, including four meta-analyses. The author mentions that the instruments more widely used included scales, subscales, inventories and questionnaires on depressive symptomatology, together with investigator-authored items or questions, but did not include the names of all the instruments in the review. The review shows evidence of significant correlations, from low to middling magnitude, between childhood sexual abuse and depression in adult life. Child sexual abuse, however, is also associated with several other psychiatric disorders, therefore having suffered sexual abuse in childhood may not be a specific risk factor for the development of depression. Clinical populations present higher effect sizes than other populations regarding the variables that mediate this relationship. Abuse with physical contact and abuse with consent generate stronger effect sizes than abuse without physical contact. The reviews analysed do not confirm an important role of other aspects in this association, such as younger age when abused, incestuous forms of abuse, use of force, higher frequency and higher duration of abuse. The limitations include the fact that, since most studies were retrospective, the results depend on the memories of the subject, which may be dysfunctional because of the very associated pathology. Besides, the investigator's interest in the relationship between current psychopathology and past abuse may generate false positives. The author also mentions as a limitation the lack of control over other kinds of possible simultaneous abuse, which may be related to current symptomatology.

The systematic review by Martins et al. (2011) investigated the association between the presence of stressors in childhood and psychiatric disorders in adult life, analysing 31 articles published between 1990 and 2010. The definition of ELS proposed by the authors included neglect and physical, sexual, emotional and psychological abuse, as well as other psychosocial stressors (e.g., parental loss, deprivation, divorce). The instruments most commonly used to evaluate childhood stressors were the *Childhood Trauma Questionnaire* (six studies) and the *Conflict Tactics Scale* (four studies), followed by the *Abuse Questionnaire*, the *Screening Survey of Children's Exposure to Community Violence*, the *Self-Report Sexual Life*, the *Traumatic Antecedents Questionnaire* and the *Childhood Trauma Interview*; some studies also used retrospective interviews and police reports. The most common types of abuse found were sexual

abuse (36.25 % of the articles), physical abuse (27.5 %), emotional abuse (11.25 %), physical negligence (8.75 %), emotional negligence (8.75 %) and general negligence (7.50 %). Once again, sexual abuse was the most studied kind of abuse during the last twenty years. A significant association was found between the presence of some kind of ELS and the presence of some psychiatric disorder in 94 % of analysed publications. The disorders most frequently present were anxiety disorders (including agorafobia, panic disorder, social phobia, specific phobias and post-traumatic stress disorder), followed by mood disorders and alcohol dependency. Important associations were also found between suffering sexual abuse in childhood and the development of schizophrenia and borderline personality disorder. The authors highlight as a limitation that the analysed studies used different concepts of ELS, for some studies, besides the most frequent kinds of maltreatment (sexual, physical or psychological abuse and negligence), also include stressors such as the presence of psychiatric disorders in the family, the loss of a family member, intrafamilial violence and economic hardships.

Hillberg et al. (2011) studied the relationship between child sexual abuse and adult psychopathology in seven meta-analysis published between 1985 and 2011. Besides noting that the most frequent instruments were face-to-face interviews and questionnaires, the authors did not provide further details on specific instruments. All meta-analysis showed that persons who suffered sexual abuse as children presented heightened risk for the development of psychopathologies compared with people who did not suffer such abuse. Effect sizes, however, were mixed, being higher in the relationships between sexual abuse in childhood and borderline personality disorder, PTSD, depression and anxiety symptoms. However, since several psychiatric disorders and symptoms are linked to childhood sexual abuse, the authors considered abuse an unspecific factor to the development of psychopathologies. Among the moderating variables analysed by the studies are sample size and sample kind, with larger samples and clinical samples showing the highest effect sizes. The studies suggest the nonexistence of gender differences in the development of psychopathologies in adult life, but that there is a significant gender difference in self-response scales regarding the psychological difficulties following the abuse.

Maniglio (2011) investigated the role of childhood sexual abuse in the etiology of substance abuse-related disorders in a review that included six publications (four systematic reviews and two meta-analysis), selecting only articles with high methodological quality. Instruments utilized were inventories, scales, subscales, questionnaires and investigator-authored items. A low to medium association between childhood sexual abuse and several disorders related to the use of psychoactive substances was found in the reviews. There was a strong relationship between childhood sexual abuse and alcoholism in women, but the same was not true for men. Childhood sexual abuse seems to be an unspecific risk factor for several kinds of substance-related disorders, since it also relates to several other psychiatric disorders. An important limitation of this study was the presence of confounding variables, given the multifactorial complexity of the etiology of substance abuse disorders. Methodological limitations in the studies included in each review, such as transversal and retrospective procedures, also prevented the establishment of a direct causal relationship.

The review by Norman et al. (2012) analysed the consequences of non-sexual maltreatment (negligence and physical and emotional abuse) upon the health of children, selecting 124 articles published until June 2012. Instruments utilized to

evaluate abuse-related symptoms were self-report questionnaires, SCID, CIDI and structured interviews, among others. The authors found robust evidence of an association between physical abuse and depressive, anxiety and eating disorders. Emotional abuse and negligence were associated with substance abuse disorders, as well as with depressive and anxiety disorders. A gender difference was found in alcohol abuse, which was linked to physical abuse in men and to negligence in women. The authors underlined limitations such as the discrepant definitions of abuse utilized in the studies, as well as the lack of randomization methods in some observational studies' group distributions.

Maniglio (2013a) investigated the role of childhood sexual abuse in the etiology of anxiety disorders in reviews published between 1996 and 2010, including four meta-analysis. The author did not specify which instruments were used for assessment, only listing general categories such as inventories, scales, questionnaires, interviews and items/subscales of questionnaires, scales or clinical inventories. The association between childhood sexual abuse and anxiety symptoms such as posttraumatic symptoms, obsessive-compulsive symptoms and phobic symptoms was significant, from low to medium magnitude. Phobic symptoms showed a statistically less significant link to several anxiety disorders when compared to other symptoms, such as posttraumatic symptoms. Therefore, it is possible that childhood sexual abuse is a more relevant risk factor for some anxiety symptoms than to others. The author discussed the effect magnitude differences found in the publications, mentioning that studies with non-clinical subjects, especially those with university students, show a smaller effect size than studies conducted with psychiatric populations. Other intervening variables such as gender, sample size and socioeconomic status were not significant in determining effect sizes. The evidence suggests, furthermore, that students who underwent intrafamilial abuse and women who suffered abuse, consented or not, may be at a higher risk of presenting anxiety symptoms. The author also mentions limitations such as methodological problems in the evaluated studies, for instance inappropriate methods to establish causality, and the lack of well-established instruments for symptom assessment. Most studies also did not control for the simultaneous occurrence of sexual abuse and other kinds of maltreatment, such as physical and emotional abuse.

The review by Maniglio (2013b) investigated the association between childhood sexual abuse and bipolar mood disorder in children and adults, analysing twenty articles published between 1995 and 2011. The instruments most commonly utilized to evaluate bipolar disorder were the *Structured Clinical Interview* (SCID; seven studies) and DSM IV charts (six studies), while the evaluation of childhood sexual abuse relied on interviews (seven studies) and the *Childhood Trauma Questionnaire* (CTQ; three studies). The publications analysed indicated that persons with bipolar mood disorder report more experiences of childhood sexual abuse than healthy controls, but report such experiences at levels similar or lower than people with other psychopathologies such as depression and schizophrenia. The prevalence of childhood sexual abuse in adults with bipolar disorder was two times higher than in children with the disorder. The author suggests that this may happen because children have not yet gone through the "risky" age for sexual abuse, or because children may not report abuse situations because they fail to recognize them as such, or even because they may not recall them well because of the many symptoms of the disorder. Some studies also interviewed parents in order to identify the abuse, but they may have failed to report the

abuse because of their lack of knowledge or intrafamilial characteristics. No statistically significant gender differences related to the frequency of childhood sexual abuse were found. The author also mentions that it is not surprising that individuals with psychopathologies report higher levels of sexual abuse than healthy individuals, since childhood sexual abuse is a risk factor for the development of psychopathologies. While we may hypothesize that a relationship between childhood sexual abuse and bipolar mood disorder exists, the limitations of the review make it impossible to establish that this traumatic event is etiologically responsible for the bipolar disorder. Such limitations include studies with samples that are not representative of the general population, studies which do not control for whether the abuse happened before or after the appearance of the symptoms of bipolar disorders, and the lack of controls for comorbidities.

4 Discussion

The reviews analysed here highlight important evidence of the association between stressful childhood experiences and cognitive and neurobiological development. Several kinds of subjects, such as children, adolescents and adults, both from healthy and clinical populations were included and several kinds of maltreatment in these populations were analysed in a broad chronological spectrum. The heterogeneity in terms of subjects, objectives, places and time of the included studies provides us with a broad view of the several aspects regarding childhood maltreatment. It is important to highlight that most trials were retrospective studies, comparing maltreated persons and controls. Therefore, rather than establishing a causal relationship between maltreatment and negative developmental impacts, this review analysed the association between these factors.

More studies regard an impaired neurobiological development in adults than in children, so that the evidence of a long-term difference in development is better known. All reviews discussed here showed a series of negative neurobiological development, both neuroendocrine, structural and functional, associated with several kinds of maltreatment. The most evident neuroendocrine alteration is in cortisol concentration levels in maltreatment victims, which is either higher or lower than expected, suggesting a misregulation of the HPA axis, responsible for leading the person to alostasis. There is also a higher concentration of neurotransmitters such as dopamine, adrenaline and noradrenaline, linked to a chronic heightened response to stressors. Regarding structural alterations, most studies show a reduction of several brain structures in adults who suffered maltreament as children, with a negative global effect on the victims' brain development. The most important functional alteration found was a hiperactivation of the amygdala, present particularly in women who suffered sexual abuse.

Only two systematic reviews about the association of childhood maltreatment and cognition were found, of which only one regarded this issue directly and was published recently. This review, conducted by Irigaray et al. (2013), analysed few publications, mostly dealing with child samples. The articles included showed discrepant results for both child and adult samples, even though they showed important cognitive deficits in children who suffered several kinds of maltreatment. There is, in a general way, evidence for a negative global cognitive association with childhood maltreatment, both

short and long-term, and above all in memory and in the several executive functions. However, Irigaray et al. (2013) also point out that few articles about this issue were found and that most of them had only adult women in their samples. Sample size was also generally small. Therefore, the determination of which kinds of maltreatment is associated with which cognitive domains in a more specific manner still has to be more intensively studied, particularly with child samples. The second review included here dealt with the cognition of homeless children and adolescents. Although not focusing on the impact of childhood maltreatment on cognition, the review provided data regarding the association with physical and sexual abuse. A comparison of the cognitive sequelae of children who suffered only physical abuse, only emotional abuse, and both kinds of abuse, points to a greater cognitive deficit, particularly of attention, in victims who suffered more than one kind of abuse. Therefore, exposure to more than one type of violence seems to have a specific impact on cognition, which has received very little attention in scientific literature.

Among the issues discussed in this study, the association between childhood maltreatment and the development of psychiatric disorders is the one that has received the most attention in the last few decades. Anxiety disorders (including PTSD), mood disorders and alcohol abuse are the disorders most frequently associated to any kind of maltreatment. More specifically, verbal abuse is linked to the development of several personality disorders in adult life, such as borderline, narcissistic, paranoid, schizoid and schizotypic disorders. Emotional abuse has been consistently linked to the development of schizophrenia in adulthood, and sexual abuse with borderline personality disorder. Physical abuse is associated to a five-time increase in the probability of developing bulimia nervosa.

Generally, reviewed studies show that childhood maltreatment relates to a series of neurobiological and cognitive damages, as well as psychiatric symptoms. Despite the fact that these consequences occur together with individual maturation and development, not much attention has been given to the understanding of this phenomenon in an integrative fashion (Pechtel and Pizzagalli 2011). The neurobiological damages result both in cognitive deficits and in difficulties in emotional regulation, which might leave the person vulnerable to development of several psychiatric disorders.

Among the limitations of the studies included in this review, the most important was the lack of a clear definition of the several kinds of maltreatment and of the subtypes of ELS. Even though most studies use the WHO's definition presented in the introduction and use instruments that evaluate physical, sexual and emotional abuse and negligence, some studies mentioned in the reviews included the loss of family members and economic difficulties as equally relevant stressors. It is known, moreover, that the sequelae depend on the kind of maltreatment, the number of events and their severity. There is also an important effect of age at the beginning of the traumatic events (Pechtel and Pizzagalli 2011). Few of the studies from the analysed reviews controlled these variables. Most of the included studies were also retrospective studies, and the samples of the empirical studies varied greatly regarding the age at the beginning of the traumatic events and the type and severity of trauma. The establishment of causal relationships might be possible in the future, if more prospective studies appear in systematic reviews about the outcomes of child maltreatment.

Despite these limitations, we were able to integrate the broad range of outcomes regarding neurobiological alterations, cognitive deficits and emotional alterations

distinctive of psychiatric disorders in victims of childhood maltreatment. We recommend that both researchers and clinicians pay attention to the intimate feedback-driven relationship between these outcomes, what suggests the utilization of multimodal treatments. Further reviews of prospective studies with clear definitions of ELS and child maltreatment might aid in explaining the relationship between the possible outcomes of such events. Only with a solid knowledge about this relationship might it be possible to intervene with preventive measures focused on children in vulnerable situations, as well as to aid health professionals in treating victims of maltreatment, lowering both its short- and long-term deleterious impacts.

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