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Paediatric Bipolar Disorder – Are Attachment and Trauma Factors Considered?

Peter I. Parry
Flinders University
Australia

1. Introduction

1.1 Debate over the boundaries of bipolar disorder

Significant debate and controversy surrounds the boundaries of Bipolar Disorder (BD). Proponents of a broader category for BD within psychiatric nosology (e.g. Akiskal, 2007) argue that more limited episodes of mood instability in both time and severity belong on a broader bipolar spectrum. Others (e.g. Paris, 2009) contend that hypomanic symptoms that fail to meet full DSM-IV or ICD-10 criteria for time or severity for BD-I and some BD-II disorders are more likely to represent reactive affective states related to environmental and relational stressors and/or personality traits or disorders. A widening of what constitutes BD beyond traditional concepts of manic-depressive illness has been related to historical and social factors impacting on psychiatric nosology (Healy, 2010).

In this context probably the most intense controversy has been over the way the borders of BD have been extended into childhood. Paediatric Bipolar Disorder (PBD), synonymous with "Juvenile Bipolar Disorder", has been described in an editorial (Ghaemi & Martin, 2007) in the *American Journal of Psychiatry* as "notoriously controversial, with the epicentre of the debate being whether the condition can be diagnosed in pre-pubertal children at all."

1.2 Historical perspective on PBD

1.2.1 Pre-1995 perspectives

In antiquity the term "mania" historically was applied to any state of frenzied madness or marked behavioural dyscontrol and, as Healy (Healy, 2008 p.7) illustrates, the manic states described by Hippocrates were essentially states of delirium accompanied by fever. According to Healy (2008, p.56) mania was not described in the context of manic-depressive illness until the mid 19th century by Baillarger in France and it was not until Kraepelin at the dawn of the 20th century that the term gained its widespread modern psychiatric usage.

Kraepelin noted amongst his 900 cases of manic-depressive psychosis that the disorder could have onset in adolescence but cases with onset prior to age 10 were sporadic with a rate of 0.4% (Silva et al., 1999). Traditionally BD has been viewed as having its onset in late adolescence to young adulthood. Rare sporadic pre-pubertal cases were described, but it wasn't until the 1980s that articles appeared raising the question that childhood onset cases

of BD may present atypically and could be being missed (Carlson, 1984). However clinical practice did not alter until after the appearance of a series of articles in the mid 1990s.

1.2.2 Post-1995: The "narrow" and "broad" PBD phenotypes

Two articles published in 1995 sought to redefine mania and BD as presenting in atypical but reliably measurable ways in children and adolescents. Researchers at Washington University in St Louis (WUSL) characterised mania in children as presenting with prolonged episodes of "ultradian" (several times per day) cycling of mood episodes (Geller et al., 1995), meanwhile a group from the Massachusetts General Hospital affiliated with Harvard (MGH/Harvard) (Wozniak et al., 1995) characterised mania in children as presenting with chronic irritability generally without distinct time limited mood episodes.

The *Journal of the American Academy of Child and Adolescent Psychiatry* has given PBD prominence in major reviews (Geller & Luby, 1997; Pavuluri et al., 2005; Kowatch et al., 2005; Liu et al., 2011) and a report on the National Institute of Mental Health (NIMH) "research roundtable on pre-pubertal bipolar disorder" (Nottelman, 2001). The NIMH research roundtable defined the two subtypes as "narrow phenotype" (WUSL) and "broad phenotype" (MGH/Harvard).

1.2.3 Rise in diagnostic rates of PBD

Following this academic lead the number of children and adolescents diagnosed with PBD in the USA skyrocketed. Community rates of BD diagnosis in the paediatric range increased 4,000% from 1994-5 to 2002-3 (Moreno et al., 2007) and PBD became the most common diagnosis in US preadolescent psychiatric inpatient units by 2004 (Blader & Carlson, 2006).

Blader and Carlson cited "diagnostic upcoding" as a major driving force for the increased rate of PBD diagnosis. "Diagnostic upcoding" occurs when factors extraneous to the patient's condition provide benefit for a particular diagnosis. These factors mainly involve the way health insurers fund health care based on diagnosis rather than clinical need. Thus a child with ADHD and Oppositional Defiant Disorder (ODD) or Conduct Disorder (CD) may be having serious problems relating to his family and school and need an inpatient evaluation, but the inpatient evaluation might only be funded if there is a diagnosis of BD. There has been less diagnosing of PBD outside the USA (Parry et al., 2009), perhaps because most other developed countries do not link mental health care so directly to DSM diagnoses.

The epidemiology of PBD is worthy of further study in itself as vastly differing rates of diagnosis have been found for mainly cross-sectional and retrospective recall studies. The diagnostic rate depends greatly on the criteria used by the researchers no matter where the studies are done (Van Meter et al., 2011) and thus reflects differing viewpoints and does little to assist resolution of the controversy. However a retrospective recall study of adults with BD reflected the international divergence: 2% of Dutch and German subjects reported pre-teen onset, whilst 22% of the USA cohort reported pre-teen onset (Post et al., 2008).

1.2.4 "Severe mood dysregulation" (SMD)

Follow-up studies of youth diagnosed with "broad phenotype" PBD have shown they are no more likely to progress to adult BD than the general population. This has led to a

renaming of this group as exhibiting "Severe Mood Dysregulation" (SMD) (Brotman et al., 2006; Dickstein et al., 2006; Stringaris, 2009 & 2011; Leibenluft, 2011).

1.3 A controversial diagnosis

The validity of PBD has been subject to vigorous debate in the literature and media (Parry & Allison, 2008) and described as a "fad diagnosis" in "epidemic" proportions by the head of the former DSM-IV task force (Frances, 2010). Psychiatrists have published books for parents both for (e.g. Papolos & Papolos, 2000; McDonnell & Wozniak, 2008) and against (Kaplan, 2011) the diagnosis. Kaplan argues diagnoses such as ADHD and ODD/CD often suffice without recourse to a "comorbid" PBD diagnosis.

The relationship of the pharmaceutical industry and psychiatry has been a focus of concern in recent years (Freedman et al., 2009). The PBD diagnosis has been a particular focus of this debate (Frances, 2010; Parry & Levin, 2011; Levin & Parry, 2011; Robbins et al., 2011).

The controversy surrounding PBD intensified following a much publicised and tragic medication related death of a 4 year old girl, Rebecca Riley, in Boston in 2006. In the wake of the tragedy, the Boston Globe reported that both Rebecca's 6 year old sister and 11 year old brother and both her parents were also diagnosed with PBD and BD. Also there was a litany of child protection notifications, including the battering of her brother by their father and that her 13 year old half-sister had been removed by child protection services due to alleged sexual abuse also by Rebecca's father (Cramer, 2007). In the wake of the tragedy vigorous debate about PBD amongst researchers and clinicians spilled into the public media. Van der Kolk, a Harvard professor prominent in traumatology research, was quoted saying: "the (PBD) diagnosis is made with no understanding of the context of their life" (Carey, 2007).

1.4 Alternative perspective: Attachment insecurity and developmental trauma

Thus one of the main critiques of the construct of PBD is that it has arisen from and compounded a neglect in psychiatric nosology of attachment insecurity and developmental trauma in the lives of children and adolescents (McClellan, 2005; Harris, 2005; Carlson & Meyer, 2006; Parens & Johnston, 2010; Parry & Levin, 2011).

To date there has not been any systematic literature review to test whether in fact this is the case. This chapter therefore explores whether developmental contextual factors have been neglected, through a systematic literature review of the presence of attachment theory and developmental trauma and maltreatment concepts in the PBD literature.

2. Methods

A systematic review of the literature was conducted using the Scopus academic search engine. Scopus allows for searches for specific words within large numbers of selected articles, which aids this type of literature review. Searches can be in various fields such as title, abstract and/or keywords. In particular an "All Fields" search with Scopus should detect a word when it is in the article's title, keywords, abstract and list of citations/references titles. The search covered the period from January 1995 to June 2010.

2.1 Defining a body of PBD literature

A body of PBD literature was defined by a Scopus search in "Title-Abstract-Keyword" fields for [*pediatric* or *paediatric* or *juvenile* or *early-onset* or *adolescen** or *teenage** or *child** or *youth* or *kids*] and [*bipolar* or *mania* or *manic* or *hypomania* or *hypomanic* or *manic-depression* or *manic-depressive*] for publications since 1995 to 15 June 2010. This gave rise to 7,257 articles, though with low specificity for PBD articles. In Scopus an "All Fields" search detects a word in the article's list of citations as well as in title, keywords, and abstract. From the 7,257 articles an "All Fields" search for the word "attachment" found 165 articles of which 15 were PBD oriented. Full texts of these 15 articles were examined for context of the word "attachment".

To obtain a more specific body of PBD literature a Scopus search was conducted in "Title-Abstract-Keyword" fields for permutations of: [*pediatric* or *paediatric* or *juvenile* or *youth* or *child** or *early* or *adolescen** or *teenage**] (with and without *"onset"* or *–onset*) and [*bipolar* or *mania* or *hypomania* or *"manic depression"*] also [*bipolar* or *manic* or *hypomanic*] and [*child** or *teen** or *"adolescen** or *youth* or *kids*] also [*bipolar* or *mania* or *hypomania* or *"manic depression"*] and [*"in a" – child* or *boy* or *girl* or *adolescent*] also [*child* or *boy* or *girl* or *adolescent* – *"with"*] and [*bipolar* or *mania* or *hypomania* or *"manic depression"*].

As of 15 June 2010 the search found 1,113 publications. Perusal indicated high specificity to articles relating to PBD. This subset of PBD literature was then subjected to a Scopus "All Fields" search. To ascertain whether attachment theory and trauma aspects were considered, a search for the terms *attachment, trauma* (also detects posttraumatic/traumatized etc) or *PTSD* or *maltreatment* or *abuse* was conducted.

2.1.1 PBD literature from "narrow phenotype" and "broad phenotype" researchers

From the PBD literature of 1,113 articles, two subsets of literature were defined by affiliation with the two academic child psychiatry departments that first promoted PBD: WUSL and MGH/Harvard. Given the question of how much the PBD literature considered attachment theory and trauma factors, literature from institutions that had historically most influenced the PBD literature should give some important indication as to the question of incorporation or otherwise of attachment theory and trauma concepts. There were 64 articles affiliated with WUSL, and 137 articles affiliated with MGH/Harvard. No articles were affiliated with authors from both institutions. Full texts of 198 of these 201 publications were downloaded and manually searched for the terms – *attachment, trauma, PTSD*, *maltreatment*, *abuse*, and *neglect*. Only 3 articles were accessible by just abstract and citation list.

2.1.2 Attachment theory literature

A body of attachment theory related literature was defined by Scopus search in "Title-Abstract-Keywords" for ["*attachment theory*" or "*attachment security*" or "*attachment insecurity*" or "*avoidant attachment*" or *"secure attachment"* or "*insecure attachment*" or "*ambivalent attachment*" or "*disorganised attachment*" or *"reactive attachment"* or *"resistant attachment"* or "*attachment disorganisation*" or "*developmental psychology*" or "*developmental trauma disorder*" or "*developmental neurobiology*" or *"developmental psychopathology"* or *Bowlby*] resulting in 4,583 publications from 1995 to 13 June 2010. To aid specificity the above terms were searched in "Title" field only, to give a sample of 746 publications.

This "attachment theory related literature" was searched for the presence of PBD terms by searching within "All Fields" for ["*pediatric bipolar*" or *"pediatric onset bipolar"* or *"pediatric onset bipolar"* or "*paediatric bipolar*" or *"paediatric onset bipolar"* or "*juvenile bipolar*" or *"juvenile onset bipolar"* or "*early-onset bipolar"* or "*child* onset bipolar*" or "*child* bipolar*" or "*adolescen* bipolar*" or "*adolescen* onset bipolar*" or *teenage* bipolar"* or *"teenage* onset bipolar"* or "*pediatric mania*" or "*pediatric hypomania*" or "*paediatric mania*" or "*paediatric hypomania*" or "*juvenile mania*" or "*juvenile hypomania*" or "*early-onset mania*" or "*early-onset hypomania*" or "*child* mania*" or "*child hypomania*" or "*adolescen* mania*" or "*adolescen* hypomania*" or "*teenage* mania*" or "*teenage* hypomania*" or "*youth mania*" or "*youth hypomania*"]. Specific terms such as these were used to define publications that specifically referred to PBD rather than publications relating to offspring of adults with bipolar disorder. Only 8 articles were found.

3. Results

3.1 "Attachment", "PTSD/trauma" and "maltreatment/child abuse" in PBD literature

In 1,113 articles on PBD there were just 14 publications with the word "attachment"; 29 publications with "trauma/PTSD"; and 64 publications containing at least one of "maltreatment/child abuse/sexual abuse/physical abuse/emotional abuse" in an "All Fields" search. With overlap this amounted to 84 publications in total (Figure 1).

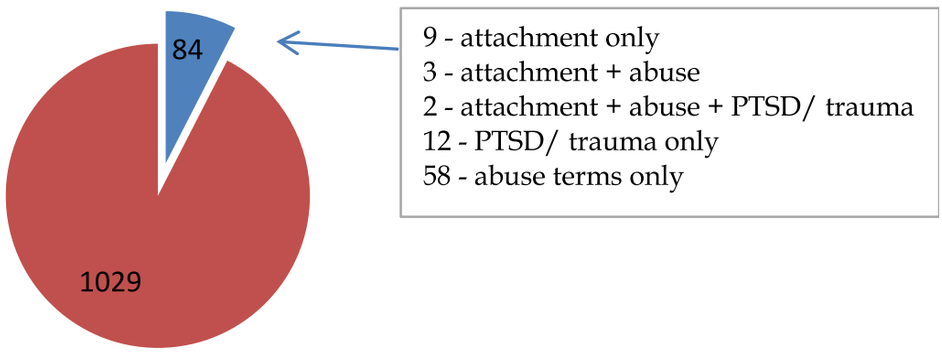

Fig. 1. Attachment and maltreatment/trauma terms in the PBD literature.

3.2 Fifteen PBD articles mentioning "attachment"

10 of the 14 articles that found "attachment" in the "all fields" search were PBD oriented, 4 related to (non-PBD) offspring of bipolar parents' studies. A further 5 articles were found from the less specific list of 7,257 articles. Thus 15 full-text articles were examined and the word "attachment" was used in the following contexts:

3.2.1 Attachment related concepts as a significant theme (3 articles)

A case study (Bar-Haim et al., 2002) of a 7 year old boy with multiple neurodevelopmental delays and diagnoses of PBD, ADHD and ODD included an attachment perspective. An article on family therapy for PBD children (Miklowitz et al., 2006) accepted the validity of PBD phenotypes but promoted family therapy approaches. A review of PBD (Carlson & Meyer, 2006) was critical of over-diagnosis of PBD, noting that PBD research "would benefit from a developmental psychopathology perspective".

3.2.2 Attachment in text as minor theme (5 articles)

An American Academy of Child and Adolescent Psychiatry (AACAP) research forum on early-onset bipolar disorder (Carlson et al., 2009) contained a passage on contextual issues, maltreatment and family dysfunction. The article mentioned "insecure attachment" as a "risk factor for emotional dysregulation and externalizing disorders" among offspring of parents with bipolar disorder. This was one of the very few documents to use the term "maltreatment" and "insecure-attachment", though there was no specific mention of neglect or PTSD. The research forum also noted: "low socioeconomic status, stressful life events, cognitive style, negative hostile parenting as reflected in low maternal warmth, poor social supports, parent divorce and conflict and physical and sexual abuse have all been identified as risk factors for development of EOBP (early onset bipolar disorder)."

Dickstein and Leibenluft (2006) reviewed differences between "narrow phenotype" PBD and "severe mood dysregulation", including neuroimaging differences and referred to attachment theory based neurobiology research. The article mentions concepts from the attachment theory based literature e.g. the importance of facial gaze in mother-infant dyads.

A personal perspective on a career in child psychiatry (Cytryn, 2003) noted "insecure attachment" was found in a small prospective study of offspring of mothers with bipolar disorder. The offspring developed psychiatric disorders but not PBD.

McClure et al. (2002) expressed caution about the validity of PBD diagnoses and advocated for attachment perspectives in history taking and observations of child-family interactions.

A summary (Parens & Johnston, 2010) of a workshop on "controversies surrounding bipolar disorder in children" had "attachment" in a citation title and once in the text: "…workshop participant and child psychiatrist Mary Burke speculated that, in the underprivileged community where she practices, one of the most effective ways to help children now receiving the BP diagnosis would be to promote attachment and reduce stress on families."

3.2.3 "Attachment" only in a citation title (5 articles)

A review (Post & Leverich, 2006) of psychosocial stress as a risk factor for earlier onset and worsened course of bipolar disorder, discussed the ameliorating influences of psychotherapy and psychoeducation. "Attachment" was mentioned in the title of a reference (Insel) which was used in a text description of animal attachment oriented studies, noting that these studies: "should make one extremely cautious in ascribing what appear to be genetic predispositions to genes, as opposed to familial/environmental influences that can themselves determine lasting neurobiological and behavioral traits."

A study (Meyer et al., 2006) of the Wisconsin Card Sorting Test in adolescent offspring of mothers with bipolar disorder had "attachment" in a citation title (Cicchetti) which was referenced in the passage: "Our results suggest that early exposure to extreme levels of maternal negativity appears to increase the risk for apparent frontal lobe dysfunction, which in turn, heightens vulnerability for the development of bipolar illness. This suggests that prevention efforts with high-risk families should go beyond children's symptomatology to focus on ways of improving the environments in which they are developing."

An article (Costello et al., 2002) that discussed abuse and parenting as minor themes had "attachment" in a citation title (Nachmias) which was used as a reference for: "evidence suggests that responsive caretakers may buffer the risk for depression and other forms of psychopathology". Another (Hirshfeld-Becker et al., 2003) had "attachment" in a citation title (Mannassis), which was referenced with others to say "some studies find an association between behavioral inhibition and anxiety disorders", and a fifth (Petti et al., 2004) had "attachment" in a citation title which was referenced in relation to a life events checklist that did not address attachment concepts, though social relationships were discussed.

3.2.4 "Parent-child relationship" as a keyword synonym for "attachment" (1 article)

The keyword "parent-child relationship" as a synonym for "attachment", appears to have led Scopus to choose an article (Schenkel et al., 2008) that stated: "Compared to controls, parent–child relationships in the PBD group were characterized by significantly less warmth, affection, and intimacy, and more quarreling and forceful punishment."

3.2.5 "Reactive Attachment Disorder" (1 article)

One article (Marchand et al., 2005) did not refer to attachment theory, but to "Reactive Attachment Disorder" in the DSM-IV sense. However the article focused on trauma and complex PTSD as differential diagnoses to PBD, noting: "children with symptoms suggestive of bipolar disorder must be carefully screened for exposure to adverse events."

3.3 Full text searches of two academic centres prominent in PBD research

The above search for attachment, trauma and maltreatment terms was in "All Fields" so would not detect terms if in articles' text but not in title, abstract, keywords or citations. There were 201 articles from authors affiliated with WUSL (research centre to first propose "narrow phenotype" PBD) and MGH/Harvard (research centre to first propose "broad phenotype" PBD). These were full text searched.

3.3.1 PBD literature affiliated with WUSL

Eleven of 64 articles contained at least one of the searched terms except for "maltreatment".

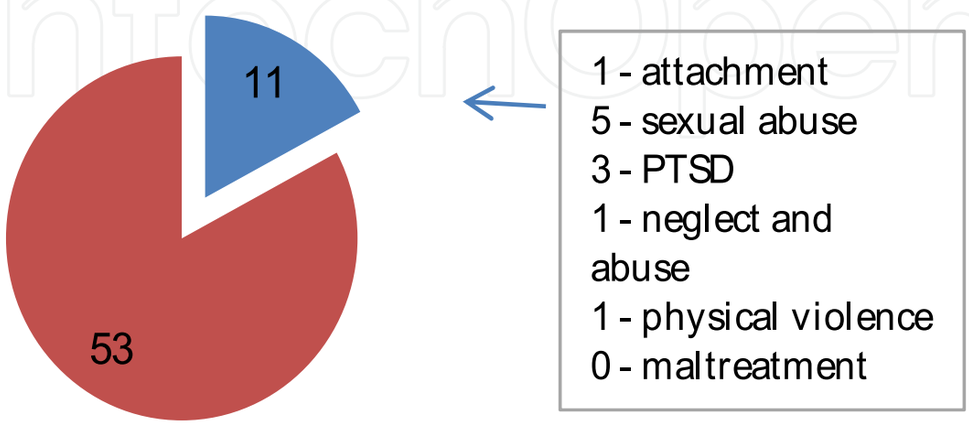

Fig. 2. Attachment and maltreatment/trauma terms in WUSL PBD literature.

As previously mentioned (Petti et al., 2004) contained "attachment" in a citation title. However though discussing the child subjects' social and family relationships, the article didn't address attachment per se in the text.

Five articles (Geller & Luby, 1997; Geller et al., 2000; Geller et al., 2002; Craney & Geller, 2003; Geller, Tillman, Badner, & Cook, 2005) contained the term "sexual abuse". These referred to "sexual abuse" as a differential diagnosis for "manic hypersexuality". They concluded that as only 1.1% in the cohort of 93 children with PEA-BP (prepubertal and early adolescent onset bipolar disorder) had "sexual abuse or overstimulation", whereas 43% (particularly the children who had hit puberty) had "manic hypersexuality" this "strongly supports hypersexuality as a symptom of mania" (Geller et al. 2002).

PTSD was mentioned (Geller et al., 2004) in a list of potential differential or comorbid diagnoses for the cohort of 93 (86 at follow-up), noting no cases of PEA-BP had PTSD. Another article (Geller et al., 2009) also mentions zero cases of PTSD in a diagnostic list for forty-seven 14 year old PBD subjects in a neuroimaging study. A further article (Luby & Navsaria, 2010) had PTSD in a citation title but PTSD/trauma was not mentioned in the text.

The terms "physical violence" and "sexual abuse" were listed in a "Life Events Checklist" and noted that with the cohort of 93 PEA-BP children there were significantly more adverse life events than for both ADHD and normal control groups (Tillman et al., 2003). The authors concluded: "Because there was no a priori reason to expect significantly more independent life events in the PEA-BP compared to the ADHD and NC groups, these results warrant further research into the role of life events in the onset of PEA-BP."

A study (Luby & Beldon, 2003), of 21 "Bipolar I" depressed preschoolers compared with 54 unipolar depressed preschoolers diagnosed by the PAPA (Preschool Age Psychiatric Assessment that is based on DSM-IV), mentioned "neglect" and "abuse" in the following context: "adverse environmental outcomes include neglect and/or abuse as well as psychosocial stressors and trauma". They concluded: "the finding that preschoolers with this bipolar syndrome did not experience greater trauma or adverse life events than other groups is also of importance. While this does not confirm the syndrome is a bipolar disorder, it does suggest that it cannot be explained by developmental deviation secondary to trauma, as has been widely speculated. However, longitudinal follow-up data will be needed to more definitively clarify this nosologic issue". The authors did note a limitation of the study was: "Findings are also limited by sole reliance on parent report of symptom states, frequencies and duration".

One article (Craney et al., 2003) didn't mention attachment theory by name, but did note that 2 year follow-up research with the PEA-BP cohort of 93 children found "low maternal warmth" the only predictive factor for relapse of mania. The risk was strong: "subjects with low maternal–child warmth were 4.1 (95% CI ¼ 1.7–10.1) times more likely to relapse after recovery (19). No other baseline characteristics (e.g. MDD, CGAS, mixed mania, continuous cycling, psychosis, ODD/CD) predicted recovery or relapse." In fact there was a 100% relapse over 2 year follow-up for those with low maternal warmth compared with 40% relapse for those with high maternal warmth. They concluded that this was a similar effect to high expressed emotion (EE) in schizophrenia, and stated: "These data from the PEA-BP sample strongly point toward the need for research on non-pharmacological modalities".

3.3.2 PBD literature affiliated with MGH/Harvard

The Massachusetts General Hospital in Boston is affiliated with Harvard University and has been the main research centre proposing "broad phenotype" PBD. Of 137 articles, 23 contained one of the searched for terms somewhere in the full text.

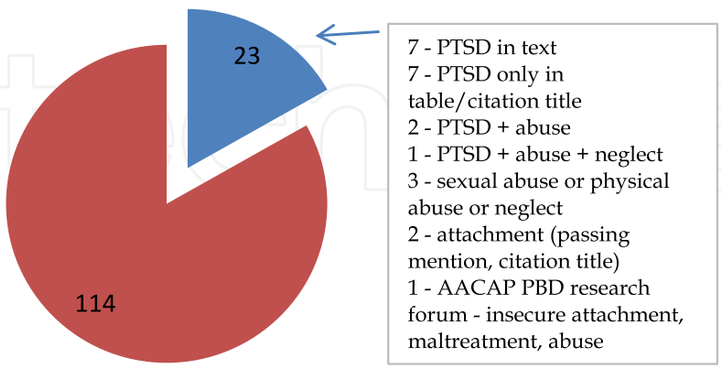

Fig. 3. Attachment and maltreatment/trauma terms in MGH/Harvard PBD literature.

The word "attachment" appears in 2 articles. One article (Henin et al., 2005) mentioned "attachments in infancy" in the passage: "the few studies that have examined the psychosocial functioning of children at risk for mood disorders have suggested that these children display poorer social skills and attachments in infancy (Zahn-Waxler et al 1984), as well as deviant school behaviors (Weintraub et al 1975, 1978), impaired academic performance (McDonough-Ryan et al 2000, 2002), suicidality (Klimes-Dougan et al 1999), and poorer peer social networks (Pellegrini et al 1986) in childhood. Taken together, these findings suggest that bipolar disorder may be characterized by extensive premorbid social and academic maladjustment."

The other (Biederman et al., 1998) mentioned "reactive attachment disorder" in a passage: "…a key limitation of our work: neither the structured interview diagnoses nor the clinical chart ratings can be accepted as unequivocal evidence for the diagnosis of bipolar disorder. For example, some of our patients met criteria for PTSD, and we did not assess for other disorders such as reactive attachment disorders that might present with manic symptoms. Thus, although our results demonstrate a link between mood stabilizer treatment and maniclike symptoms, they are not definitive as regards the treatment of bipolarity."

Neither paper elaborates upon attachment theory beyond those statements. Also the statement from Biederman et al. (1998) is somewhat at odds with the reported findings in the 16 other articles that mention PTSD. Nine of these articles only mentioned PTSD in a diagnostic list or table: in a diagnostic list of anxiety disorders (Spencer et al., 1999; Hirschfeld-Becker et al., 2006); as a comorbid diagnosis with 14% of preschool and 10% of under age 10 PBD diagnosed children (Wilens et al., 2003); as 1 comorbid PTSD case in a cohort of 18 PBD diagnosed children (Moore et al., 2007a) and 2 of 32 PBD diagnosed children (Moore et al., 2007b) and another article on the same cohort listed 2 of 28 PBD diagnosed children comorbid for PTSD (Frazier et al., 2007). Another study (Harpold et al., 2005) found high rates of all anxiety disorders within a PBD cohort and that PTSD had the highest odds ratio of correlating with PBD and concluded "our results indicate that BPD (bipolar disorder) significantly and robustly increased the risk of a broad range of anxiety

disorders in youth." A recent study (Joshi & Wilens, 2009) also found high comorbidity rates with PBD. Wozniak (2003) did refer to PTSD in the text, noting that PBD research has been criticized amongst other things for "difficulty in distinguishing bipolar disorder (BD) from other conditions marked by irritability such as attention deficit/hyperactivity disorder (ADHD) and posttraumatic stress disorder (PTSD)."

Three papers (Biederman et al., 2000; Biederman et al., 2003; Wozniak et al., 1999) that dealt with the issue of trauma and PTSD more directly in the text concluded that PBD precedes trauma and PTSD. A child with PBD is so disruptive that they create traumatic situations and family relationships that then impact traumatically upon them. Both Biederman et al. (2000, 2003) articles refer to the earlier Wozniak et al. (1999) study and contain the same passage that states: "Using data from a longitudinal sample of boys with and without ADHD, Wozniak et al. (1999) identified paediatric bipolar disorder as an important antecedent for, rather than consequence of, traumatic life events… When traumatized children present with severe irritability and mood lability, there may be a tendency by clinicians to attribute these symptoms to having experienced a trauma. To the contrary, longitudinal research suggests the opposite: mania may be an antecedent risk factor for later trauma and not represent a reaction to the trauma (Wozniak et al 1999)."

Wozniak et al. (1999) had reported: "Our results showed that the diagnosis of bipolar disorder at baseline assessment in children with ADHD was the most significant predictor of the development of later trauma during the 4 year follow-up period. Although not entirely surprising, this finding, to our knowledge, has not been previously reported. Considering that mania is a very severe disorder with high rates of explosiveness, aggression, impulsivity, and poor judgement (Wozniak et al 1995a), it could predispose an affected child to trauma exposure…If confirmed, these results could help dispel the commonly held notion that mania like symptoms in youths represent a reaction to trauma."

The Wozniak et al. (1999) study was a 4 year follow-up study of 128 boys with ADHD (of whom 14 were diagnosed on structured interview with comorbid PBD at baseline and a further 7 diagnosed with PBD at the 4 year follow-up) plus 109 normal controls of whom 2 were diagnosed with comorbid PBD at follow-up. Fifteen of the 128 experienced a traumatic event and 4 (27%) of these 15 had comorbid PBD compared to 10 (9%) rate of comorbid PBD in the 113 ADHD boys without traumatic events during the follow-up period. The authors noted limitations – "our number of trauma-exposed subjects (including controls) was relatively small (n=23), and a very small number of traumatized subjects (n =2) went on to develop PTSD. …our results should be viewed as preliminary until confirmed with larger samples." They also noted they did not assess for PTSD at baseline: "the findings reported in this study must be seen in light of methodological limitations. Since we assessed trauma only for the 4 year follow up period and did not make a lifetime assessment of trauma, we cannot rule out the possibility that trauma could have predated or contributed to the development of bipolar disorder in some children. However, if trauma were to lead to mania rather than the other way around, we should have found that children without mania traumatized during the follow-up period would be more likely to go on to develop mania. This was not the case in our study." Additionally whilst the study reported 1 child (out of 237) had experienced "physical abuse" and 3 children experienced "sexual abuse", the study does not report on any verbal or emotional abuse in the "types of trauma" examined.

The ages of the boys at the 4 year follow-up was peripubertal on average (ADHD 10.3 SD 2.9, ADHD + Trauma 12.3 SD 3.1, Control 11.5 SD 3.6, Control + Trauma 12.0 SD 4.1) and it is not reported as to what extent early life attachment factors were assessed. Wozniak et al. (1999) stated: "The literature suggests that protective factors operating at various stages of development may buffer children from posttraumatic suffering. For example, in a study of children and adults surviving Scud missile attacks in Israel, symptoms in children correlated with symptoms in their mothers. These authors concluded that maternal stress-buffering capacity plays a crucial role in minimizing suffering in traumatized preschool children (Lahor et al 1997)." Despite this passage Wozniak et al. (1999) do not appear to elaborate on parent-child relationships as mediating stress in their study. Also only parents and not children were interviewed if the child was under age 12, therefore presumably nearly all children were not interviewed at baseline.

A more recent article (Steinbuchel et al., 2009) affiliated with MGH/Harvard found an increased rate of PTSD in adolescents with PBD, though also tended to view PBD as a risk factor for PTSD. Subjects with both PTSD and PBD developed significantly more substance use disorders (SUD) and the authors concluded that "follow-up studies need to be conducted to elucidate the course and causal relationship of BPD, PTSD and SUD." Another article (Althoff et al., 2005) cautious in tone, stated: "In 2005 the idea is clearly not 'nature v nurture' but 'nature and nurture and how they interact'. Recent discoveries have shown the interaction between the serotonin transporter gene and trauma affecting likelihood of MDD and reduced by presence of positive social support. Thus far there have not been studies of specific G X E interactions with JBD." Further caution was expressed in a study (Faraone et al., 2001) of girls with ADHD and bipolarity, noting: "We did not assess for post-traumatic stress disorder (PTSD), which often is expressed with symptoms of ADHD and bipolarity. Thus, we cannot determine if cases of PTSD may have obscured our results."

A recent article (Doyle et al., 2010) reported lack of specificity in the Child Behaviour Checklist for diagnosing JBD (Juvenile Bipolar Disorder – equivalent PBD): "The items on the three scales that contribute to the CBCL-JBD profile reflect emotional and behavioral lability and distractability, i.e., items that index the capacity for self-regulation across a wide range of domains (i.e., cognitive, behavioral and affective). Further evidence for this conceptualization comes from Ayer et al. who found that the CBCL–JBD phenotype can be modeled as sharing a single latent trait with a different secondary CBCL scale purported to measure post-traumatic stress problems (PTSP). Like the CBCL-JBD phenotype, the PTSP scale is associated with suicidality and poor outcome and features a number of items overlapping with the CBCL-JBD that relate to self-regulation. Based on this analysis, the authors suggest both scales index a single dysregulatory syndrome. The fact that the CBCL-JBD phenotype taps into a trait relevant to a range of psychiatric disorders may help to explain the profile's lack of diagnostic specificity to juvenile-onset BPD in clinical studies."

Six articles mentioned the term "abuse": physical and sexual abuse were listed in a trauma list (Wozniak et al., 1999); brief mention of sexual abuse as a differential to manic hypersexuality (Soutullo et al., 2009); physical and sexual abuse briefly mentioned in relation to PTSD (Steinbuchel et al., 2009); abuse in a citation title which is referenced in the text: "findings in the pediatric (Ackerman et al., 1998) and adult (Kessler et al., 1995) literature document high rates of comorbid PTSD in bipolar subjects" (Harpold et al., 2005); a study (Baldessarini et al., 2004) reported "no history of physical or sexual abuse was found

in any case" in a cohort of 82 PBD children (73% prepubertal with 74% having "onset of first symptoms" under age 3).

Another article (Bostic et al., 1997) mentioned infants being depressed in "abusive and neglectful situations". Otherwise "neglect" is not mentioned by MGH/Harvard authors except in the context of "neglect of PBD" as a diagnosis. The term "maltreatment" is not mentioned. The AACAP 2006 Research Forum (Carlson et al., 2009) had co-authors from the MGH/Harvard group and as above did mention maltreatment and abuse by name.

3.4 PBD terms in the attachment theory oriented literature

Just 8 papers were found by Scopus search for "attachment" in "All Fields" from a body of 746 articles. However on close examination not all these articles were strong on attachment theory based themes. The main focus for 7 of these was on anxiety and depression arising out of parent-child relationships. PBD was only a major theme in an editorial (Miklowitz & Cichetti, 2006) that was more in the context of the PBD literature (the journal, *Developmental Psychopathology*, issue was devoted to PBD) rather than attachment theory. It was possibly selected by Scopus as attachment oriented because of the phrase "developmental psychopathology" in the title and text. "Sexual abuse" is in the title of a reference. The editorial doesn't contain the word "attachment", nor "PTSD/trauma" or "maltreatment".

4. Comparison of neuroimaging reviews

Given that research in both developmental traumatology and amongst PBD investigators has focussed on neuroimaging in recent years, a comparison (but in this case not a systematic review) of neuroimaging reviews from both the PBD literature and attachment/trauma literature is of interest.

Schore is a prominent author in the attachment and developmental trauma literature who has reviewed neuroimaging research data in two books (Schore, 2003a; Schore, 2003b) and a review article (Schore, 2002). The indexes of each book do not contain the word "bipolar", and "mania" is mentioned only once in each book – in reference to right orbitoprefrontal cortex (ROPFC) dysfunction. However both books focus on ROPFC dysfunction as primarily relating to impaired modulation of subcortical limbic structures and manifesting as affect dysregulation and behavioural impulsivity relating to disorders of attachment and trauma, disruptive behaviour disorders and personality disorders. The terms "bipolar", "mania/c" or "hypomania/c" do not occur in the review article.

A recent review (McCrory et al., 2011) of the neurobiological, genetic and epigenetic factors associated with childhood maltreatment also reports amygdala hyper-reactivity and reduced frontal cortical control of subcortical limbic structures. In particular fMRI studies of emotional processing of human faces in both adults and children revealed: "hyperactivity of the amygdale in response to negative facial affect." The review covers epigenetic changes that appear to underpin such neurobiological findings and the importance of secure-attachment to promote resiliency against such effects of maltreatment. Specifically it appears that "an early hostile environment contributes to stress-induced changes in the child's neurobiological systems that may be adaptive in the short term but which reap long term

costs." Additionally cognitive deficits, particularly deficits of working memory are correlated with maltreatment and institutionalization.

Interestingly the more recent PBD literature increasingly includes neuroimaging studies comparing PBD diagnosed cohorts with, for example, normal controls (e.g. Pavuluri et al., 2009a). None of the terms for attachment, PTSD or maltreatment/abuse appear in this article. Yet it describes similar findings concerning the right pre-frontal cortex and limbic system, including right amygdala reactivity and impaired right prefrontal cortical functioning, that the above reviews from an attachment and developmental trauma/maltreatment perspective describe.

5. Discussion

5.1 Attachment and trauma/maltreatment terms generally overlooked in PBD literature

A systematic review of the PBD literature via searching for the term "attachment" lends credence to critics' claims that the PBD literature in general does not address or consider attachment theory concepts. The almost complete absence of attachment theory concepts makes interpretation of trauma and maltreatment/abuse events in childhood problematic as there is evidence that attachment security/insecurity mediates the effects of trauma and abuse upon children (Cook et al., 2005). Furthermore developmental trauma, maltreatment/abuse and PTSD related concepts receive infrequent coverage in the PBD literature. The two research institutions that first promoted PBD illustrate this: researchers from WUSL report a virtual absence of PTSD in their cohort; researchers from MGH/Harvard suggest PTSD mainly arises secondary to PBD, though more recent publications from the group are more cautious.

The very low rate of sexual abuse and no cases of PTSD in the WUSL research is remarkable in any clinical cohort. It is also at odds with research (Rucklidge, 2006) on a cohort of adolescents in New Zealand that found 29.2% reported sexual abuse on the same diagnostic instrument used in diagnosing the WUSL cohort, and over 50% of the New Zealand PBD sample had a trauma history compared with 10% of controls.

The MGH/Harvard group propose that PTSD where it does occur comorbidly with PBD arises secondary to PBD itself. However the main reference for this, a study (Wozniak et al., 1999) of 128 peripubertal boys with ADHD, of whom 14 had comorbid PBD, noted several limitations of their study including that it was of low power and that trauma and PTSD were not assessed at baseline. Nor from the article does it appear that early attachment histories had been taken in depth. Nonetheless if there was increased risk for experiencing trauma in the 4 year follow-up period for the boys with ADHD and a comorbid PBD diagnosis, an alternative hypothesis, not explored in the article, would be that the boys with ADHD and comorbid PBD at baseline were in fact exhibiting symptoms of earlier developmental trauma. Such earlier developmental trauma, mediated by psychodynamic, family dynamic, behavioural learning and other environmental contextual factors, could mean the 14 boys were more vulnerable to traumatic events over the 4 year follow-up period than those with ADHD but without PBD as defined in the study's methodology. More recent articles (Althoff et al., 2005; Steinbuchel et al., 2009; Doyle et al., 2010) from authors affiliated with MGH/Harvard are more open to the possibility of trauma factors causing or exacerbating symptoms, yet still conceptualise these symptoms in terms of PBD.

5.2 SMD articles also limit mention of attachment and trauma factors

As noted above, "broad phenotype" PBD has effectively been renamed "Severe Mood Dysregulation" (SMD) (Brotman et al., 2006; Dickstein et al., 2006; Stringaris, 2009 & 2011; Leibenluft, 2011). However a reading of these 5 papers suggests attachment and trauma related factors appear to be only a limited focus thus far, of research into SMD. Furthermore SMD is likely to feature in DSM-5 under the title: "Disruptive Mood Dysregulation Disorder" (DMDD). This proposed diagnosis has drawn some intense criticism, particularly from Frances, head of the former DSM-IV task force, who has described DMDD as one of the "worst ideas" for a new DSM diagnosis (Frances, 2011). Frances also notes that DMDD has likely been accepted as "a lesser evil replacement for childhood bipolar disorder—less stigmatizing and less likely to result in reflex long term antipsychotic use." But he suggests:

> "DMDD will capture a wildly heterogeneous and diagnostically meaningless grab bag of difficult to handle kids. Some will be temperamental and irritable, but essentially normal and just going through a developmental stage they will eventually outgrow without a stigmatizing diagnosis and a harmful treatment. Others will have conduct or oppositional problems that gain nothing by being mislabelled as mood disorder. Yet others will have serious, but not yet clearly defined psychiatric disorders that require careful and patient monitoring before an accurate diagnosis can be made."

However attachment, developmental trauma and maltreatment are still not mentioned.

5.3 Attachment theory based literature fails to mention PBD

Some PBD authors (e.g. Biederman, 2003) have strongly argued that mania and bipolar disorder is not considered by researchers who come from a more traditional child psychopathology perspective. A search of the attachment theory based literature, as outlined above, does in fact suggest unawareness or dismissal of the concept of PBD. However in defence of attachment oriented studies, it could be argued that most work to date has been in infancy and early child development prior to the onset of typical DSM clinical syndromes, at least as classically defined. Much of the attachment and developmental traumatology literature is in psychology, general science and neuroscience journals, whereas the PBD literature is primarily in US based psychiatry journals. To some extent this supports the hypothesis that there are differing paradigms governing the way children with severe emotional and behavioural problems are assessed and diagnosed.

5.4 Neuroimaging: PBD or developmental trauma/maltreatment

The specific case of neuroimaging in PBD research and attachment-trauma oriented research is an example where similar findings in the attachment-trauma oriented literature appear to be interpreted differently by authors from the PBD literature, and without cross-referencing.

Neuroimaging of children with disorganized attachment and trauma histories has, amongst other findings, revealed impaired right prefrontal cortex control over a hyperactive right amygdala. This can be explained in terms of the function of these structures in attachment relationships and for survival in the face of threat (Schore, 2002a). Neuroimaging of children diagnosed with PBD (Pavuluri et al., 2009) found essentially the same findings but made no reference to attachment and trauma factors. When this very interesting data from a

technically sophisticated study was presented at the AACAP 2009 conference (Pavuluri, 2009), I and others asked during the presentation why the children could not simply have been labelled as "affect dysregulated" rather than as having bipolar disorder? The presenter agreed they could well have, but stated that if they were not described as suffering bipolar disorder then research funding would be unlikely. At the same conference similar neuroimaging findings delineated an ADHD cohort from a PBD cohort (Delbello, 2009). The research again appeared to have high technical quality, but once again it is possible that a-priori assumptions may have governed the scope of possible conclusions. When I asked during the presentation if PTSD or disorganized attachment had been considered in addition to ADHD and PBD, the presenter replied that they had not been investigated.

The rise of new and exciting technological developments in neuroimaging and epigenetics hopefully will help develop understanding of childhood developmental psychopathology. But accurate understanding is likely to only grow if a wide range of hypotheses are maintained and all contextual factors, both historical and current, in a child's life are considered. McCrory et al. (2011) in their recent review, whilst acknowledging the high likelihood of trauma preceding brain changes, advocate for this and state that longitudinal studies are needed that "allow changes in the child's environment and behavior to be measured alongside changes in brain structure and function…if we are to make even tentative inferences regarding causality."

5.5 Perspectives from different paradigms

It has been argued that science proceeds not just in terms of applying the scientific method, but within a historical and sociocultural context with implicit assumptions and belief systems that set the parameters of the research, in other words according to a prevailing paradigm (Kuhn, 1962). The prevailing paradigm governs what is considered for study and treatment and what is not. Thus even research of high intellect, internal consistency and technical quality can lead to false conclusions if the paradigm is too restrictive. Furthermore differing paradigms can co-occur and be operative in the same era.

Based on this systematic literature review plus a selective review of neuroimaging research, there does indeed appear to be a communication gulf between two different paradigmatic approaches in child & adolescent psychiatry and developmental psychopathology.

Developmental Trauma Disorder (DTD) (Van der Kolk & Courtois, 2005) is another proposed diagnosis for DSM-5. DTD has been proposed as a more accurate descriptor for many children diagnosed with PBD (Levin 2009). However DTD is not officially within the DSM-IV, whereas ADHD is and PBD has been given semi-official status under the rubric of BD-NOS (BD Not Otherwise Specified). The DSM-IV diagnoses are used to guide and constrain much of the funding for therapy and research, particularly in the USA. Thus in the neuroimaging research presented at the AACAP 2009 conference, ADHD and PBD receive consideration, but DTD and attachment and contextual factors seemingly did not.

It has been argued that one root cause of this problem lies with the atheoretical symptom focused approach incorporated within DSM-IV (Denton, 2007) and consequently mainstream psychiatry has become too detached from attachment theory, psychoanalysis and traumatology and the progress made in these fields (Dignam et al., 2010).

These factors, in conjunction with "diagnostic upcoding" pressures, the influence of the pharmaceutical industry and a societal tendency to repress recognition of trauma have been argued as fuelling the rise in PBD diagnosis rates (Parry & Levin, 2011). Rather than existing in parallel, researchers in PBD and other DSM diagnoses may likely benefit from increased dialogue with researchers from attachment theory and developmental traumatology perspectives. Furthermore attachment theory oriented research would be advanced by exploring attachment and trauma influences in DSM-IV and ICD-10 syndromes.

5.6 Signs of increasing attention to attachment and trauma factors

In 2005 the first "treatment guidelines" for PBD (Kowatch et al., 2005) did not mention attachment or trauma factors and focussed almost exclusively on pharmacotherapy algorithms in treatment for PBD, although there was an accompanying critical commentary (McClellan, 2005). In 2006, although still labelling the phenomenology as BD, the AACAP 2006 research forum (Carlson et al., 2009) did list a range of contextual environmental adversity factors as implicated in the aetiology of PBD. In 2007 an official AACAP "practice parameter" publication (AACAP, 2007) included authors who have published articles sceptical about PBD. This AACAP practice parameter combined both paradigmatic perspectives with quite differing views within the one document. It contained a section on the "diagnostic controversy" which, referencing work from both WUSL ("narrow-phenotype" PBD) and MGH/Harvard ("broad phenotype" PBD), noted that "although symptoms of early-onset bipolar disorder appear stable over time (Biederman et al., 2004b; Geller et al., 2004) [citations in original], juvenile mania has not yet been shown to progress into the classic adult disorder." The practice parameter also listed "psychotherapeutic interventions" as important in treatment and noted "dialectical-behavioural therapy may be helpful for youths with mood and behavioural dysregulation."

At the 2010 AACAP conference there were two symposia (AACAP, 2010a & 2010b) each with several papers highlighting contextual factors and stressing a more non-aetiological descriptor of "affect dysregulation" rather than using the bipolar or mania label for children with mood swings. Also in 2010, a report (Parens & Johnson, 2010) of a 2 day workshop, involving researchers in the field of PBD, records vigorous debate over the validity of the PBD diagnosis. Attachment and trauma are mentioned and paradigmatic aspects of the issue are also canvassed. Also as illustrated in the literature review above, more recent articles from researchers affiliated with MGH/Harvard have drawn attention to the need for more research into PTSD related factors.

In contrast a recent review and meta-analysis of pharmacotherapy in PBD (Liu et al., 2011) made no mention of psychotherapy, nor of psychosocial factors in diagnosis. The review noted limited efficacy of traditional mood stabilizers (Lithium and anticonvulsants) in PBD, whereas second generation antipsychotics (SGAs) had more efficacy and speculated "such results are consistent with the hypothesis that pediatric-onset bipolar disorder may represent a different subtype of bipolar disorder that could respond to different treatments than those observed in adult-onset cases." It has been often argued however that SGAs simply exert their effect via sedation (e.g. Ghaemi & Martin, 2007; Frances, 2010; Kaplan, 2011) and do not confirm a particular diagnosis as for example juvenile mania.

5.7 Implications for therapy

The debate about whether a child with severe emotional and behavioural problems has PBD, versus DTD or ADHD plus/or ODD or CD is far from academic. The choice of treatment, the risk of suffering side-effects, the child's perception of self, the family's perception of their child and the perception and behaviour of relevant others such as teachers are strongly influenced by the diagnostic label. The controversy over PBD has become impassioned because of such consequences.

Treatment guidelines (Kowatch, 2005; Liu et al., 2011) for PBD strongly promote use of psychotropic agents. PBD has been blamed for leading to an explosion, particularly in the USA, in the use of atypical antipsychotic agents and polypharmacy approaches for children (e.g. Frances, 2010; Parry & Levin, 2011; Robbins et al., 2011; Kaplan 2011).

5.8 Limitations

This systematic literature review relied on one academic search engine, Scopus, albeit one that aids this form of literature search. Defining a body of literature in a sensitive yet specific enough manner proved somewhat challenging. A full reading of all 7,257 publications would be needed to make the searches more thorough. Nonetheless the hypothesis being tested pertains to a broad trend over the past decade and a half within child and adolescent psychiatry, rather than specific researchers or scientific articles. In that sense the use of Scopus in this manner to examine broad trends can be justified. Furthermore it can be argued that full text searching the literature from two US child and adolescent academic centres most strongly associated with developing the PBD phenotypes should give a strong indication of how attachment, maltreatment and trauma factors are considered in the wider PBD literature. The systematic literature review covered the 15 ½ years to June 2010 and it is quite possible that more may have been written on attachment and trauma/maltreatment factors in the very recent PBD literature. However the PBD phenotypes have become entrenched in research and clinical practice, at least in the USA, during the time frame since the germinal articles in 1995.

6. Conclusion

Intense controversy over the validity of PBD remains despite a decade and a half of research into the postulated PBD phenotypes. A main criticism of the PBD constructs is that they fail to consider attachment theory and maltreatment and developmental trauma factors.

A systematic search of the PBD literature presented here found this to generally be the case. There was a virtual absence of consideration of attachment theory. Trauma and PTSD was described as likely secondary to pre-existing childhood mania by researchers associated with the "broad phenotype" PBD construct. Maltreatment factors were relatively absent in findings from cohorts in both "broad phenotype" and "narrow phenotype" PBD research. Furthermore attachment, maltreatment and trauma factors do not appear to be a focus of research that reconceptualises "broad phenotype" PBD as SMD.

A comparison of neuroimaging studies from attachment/developmental traumatology and PBD research shows remarkably similar findings interpreted quite differently. Two different paradigms appear operative within the field. Increased dialogue across these paradigmatic

perspectives is likely to help resolve the controversial nature of PBD. To quote Carlson & Meyer (2006), PBD research "would benefit from a developmental psychopathology perspective". This involves greater consideration of attachment insecurity and a child's psychodynamic defences against traumatic contextual factors.

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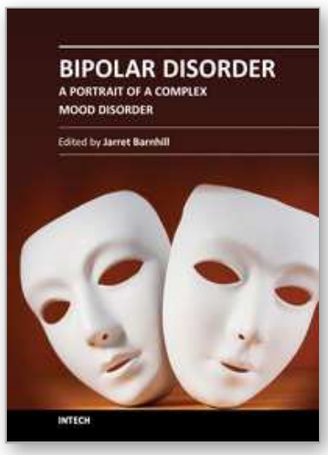

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Bipolar Disorder: Portrait of a Complex Mood Disorder is a step towards integrating many diverse perspectives on BD. As we shall see, such diversity makes it difficult to clearly define the boundaries of BD. It is helpful to view BD from this perspective, as a final common pathway arises from multiple frames of reference. The integration of epigenetics, molecular pharmacology, and neurophysiology is essential. One solution involves using this diverse data to search for endophenotypes to aid researchers, even though most clinicians prefer broader groupings of symptoms and clinical variables. Our challenge is to consolidate this new information with existing clinical practice in a usable fashion. This need for convergent thinkers who can integrate the findings in this book remains a critical need. This book is a small step in that direction and hopefully guides researchers and clinicians towards a new synthesis of basic neurosciences and clinical psychiatry

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University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
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