

REVIEW

# Attention Deficit Hyperactivity Disorder And Borderline Personality Disorder In Adults: A Review Of Their Links And Risks

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Abstract: Attention deficit hyperactivity disorder (ADHD) and borderline personality disorder (BPD) are particularly common disorders, that are highly comorbid in adult populations. The symptomatic overlap between adult ADHD and BPD includes impulsivity, emotional dysregulation and interpersonal impairment, which makes the differential diagnosis difficult. Our review aims at focusing on recent data on the comorbid ADHD+BPD form, as well as the risk factors involved in the emergence of the two disorders. While adult ADHD and BPD share some genetic and temperamental risk factors, adult ADHD is characterized by more severe trait-impulsivity compared to non-comorbid BPD; BPD patients display more severe trait-emotion regulation symptoms compared to non-comorbid ADHD. Patients with the comorbid ADHD+BPD form have severe symptoms in both dimensions. Early-life exposure to adverse events is a shared risk factor for the development of ADHD and BPD, but type and timing of adversity seem to play a differential role in the development of BPD and ADHD symptoms. Age of onset used to be a discriminative diagnostic criterion between ADHD, an early-onset neurodevelopmental disorder, and BPD, a late-onset psychological disorder. However, this distinction has been recently called into question, increasing the need for more research aiming at delineating the disorders from a developmental and clinical standpoint. Clinicians should carefully consider the comorbidity, and consider ADHD and BPD dimensionally, in order to provide more effective patient management. This might improve early preventive interventions, and treatment for comorbid conditions in adulthood.

Keywords: ADHD, borderline personality disorder, adults, emotion regulation, impulsivity

### Introduction

Attention deficit/hyperactivity disorder (ADHD) is commonly conceptualized as a neurodevelopmental disorder characterized by three clusters of symptoms – i.e., inattention, hyperactivity and impulsivity –, starting before the age of twelve according to the DSM-5<sup>1</sup> At least 50% of the children with ADHD still meet criteria for ADHD diagnosis in adulthood, and estimates of prevalence of ADHD in adulthood range from 4% to 5%<sup>2</sup> Symptomatic expressions in adults differ, however,<sup>3,4</sup> as adults may display fewer symptoms and more internalized rather than externalized forms of hyperactivity<sup>1</sup> Although not included among the core diagnostic criteria of ADHD in the DSM-5<sup>1</sup> emotion dysregulation is also very prevalent, concerning up to 70% of adults with ADHD.<sup>5,6</sup> Moreover, emotion dysregulation is among the clinical features predictive of a persistent course of ADHD symptoms in adults.<sup>7</sup>

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ADHD symptoms in adulthood greatly interfere with daily functioning, and are associated with high number of psychiatric comorbidities<sup>3</sup> Among them, borderline personality disorder (BPD) in particular is encountered far more often than expected by chance in adults with ADHD.<sup>3,8</sup> BPD is characterized by a pervasive pattern of instability in affect regulation, impulse control, interpersonal relationships, and self-image that concerns 1-6% of the general population.<sup>3,9,10</sup> BPD subjects are an heterogeneous group, with some subjects characterized by prominent dysexecutive and impulsive features, others by prominent affective or dissociative features. 11,12 At least 14% of those diagnosed with ADHD in childhood later receive a diagnosis of BPD while between 18% and 34% of the adults with ADHD are estimated to have comorbid BPD. 12-14 This along with the fact that BPD shares at least two of its symptomatic dimensions, i.e., impulsivity and emotion dysregulation, with adult ADHD<sup>15</sup> has raised the question of the nature of the relationship between the two disorders<sup>16</sup> The first two reviews focusing on this topic, <sup>17,18</sup> published prior to the DSM-5 proposal of specific diagnostic criteria for adult ADHD, concluded that there was a significant association between adult BPD diagnoses and history of childhood ADHD symptoms assessed retrospectively, hence suggesting that ADHD could represent a developmental risk factor for BPD. Three more recent reviews by Matthies & Philipsen<sup>19,20</sup> and Storebø & Simonsen<sup>16</sup> highlighted the common clinical features of BPD and adult ADHD, including impulsivity and emotion dysregulation, and the more severe forms of patients presenting with both diagnoses. However, because the interest in the overlap between adult ADHD and BPD is fairly recent, previous reviews barely addressed the characterization of the comorbid ADHD+BPD form, and only few studies included in these reviews provided a direct comparison of the clinical and neuropsychological features common to adult ADHD and BPD. Our review thus aims at filling this gap, focusing on the recent data regarding the three clinical pictures in adults, especially the comorbid ADHD+BPD form. Of major importance, age of onset used to be a discriminative diagnostic criterion between ADHD, typically viewed as an early-onset neurodevelopmental disorder, and BPD, a lateonset psychological disorder. However, this distinction has been recently called into question, increasing the need for more research aiming at delineating the disorders from a developmental and clinical standpoint.

In this study we will present a narrative review of the available data regarding i) the prevalence of the co-

occurrence of adult ADHD and BPD, ii) the clinical similarities and differences between the two groups, iii) their etiology, and iv) the developmental pathways potentially linking the two disorders. As noted above, we will focus on studies which included the adult ADHD+BPD group, and on etiological studies which might help clarifying the developmental risk factors for BPD and adult ADHD. It is crucial to gain a better understanding of the links between ADHD and BPD, to pinpoint treatment options for adults presenting with both diagnoses, but also to design early interventions to prevent the development of BPD in children and adolescents with ADHD symptoms who are at risk for BPD.

# **Epidemiologic Data On The Association Between ADHD And BPD**

By the 1980s and early 1990s, while studies confirmed the boundaries of BPD relative to affective and psychotic disorders, they also highlighted its heterogeneity, with a significant subgroup of patients presenting with a history of developmental delay and attention disorder. 11,21 Andrulonis et al<sup>22,23</sup> found that 25% of a group of 106 BPD patients with IQs greater than 80 had a current or past history of ADHD and/or learning disabilities. Similarly, van Reekum et al<sup>21</sup> reported that 27% of a group of 48 male veterans with BPD versus 6% of healthy controls had a history of ADHD. These results led the authors to suggest that there was an "organic" subgroup of patients with BPD presenting with frontal lobe dysfunction symptoms. Focusing specifically on childhood ADHD symptoms in adults with BPD, Fossati et al<sup>24</sup> showed greater retrospectively assessed ADHD symptoms via the Wender Utah Rating Scale (WURS-25)<sup>25</sup> compared to healthy controls and other personality disorders. Moreover, Fossati et al<sup>24</sup> found that 60% of patients with BPD achieved WURS-25 scores deemed as suggestive of childhood ADHD. Another cross-sectional study by Speranza et al<sup>26</sup> found 11% of ADHD in adolescent patients with BPD, and up to 46% of their sample presented at least one ADHD symptom which had some impact on functioning. Few studies have assessed the cooccurrence between ADHD and BPD longitudinally, which is crucial to understand the developmental relationship between the disorders. During the follow-up of hyperactive children into adulthood, Fischer et al<sup>27</sup> reported that 14% of their sample had developed BPD vs 3% in the control group. Similarly, Miller et al<sup>28</sup> examined the comorbidity of personality disorders longitudinally in adolescents

diagnosed with ADHD between the ages of 7 and 11. The study found that individuals with childhood ADHD were significantly more likely to be diagnosed with BPD (13.5% vs 1.2% in the control group, OR = 13.16) at the 16 to 26-year follow-up than the non-ADHD controls. Moreover, those who continued to meet diagnostic criteria for ADHD at follow-up had a higher rate of BPD diagnosis than those who remitted and controls (19% in "persisters" vs 6.3% in "remitters"). In another longitudinal study, using latent growth curve models on two cohorts of girls annually assessed between the age of 8 and 14, Stepp et al<sup>29</sup> found that higher levels of ADHD and Oppositional Defiant Disorder (ODD) scores at age 8 uniquely predicted BPD symptoms at age 14.

Recent cross-sectional studies also showed a persistent course of ADHD symptoms in a high number of adults with BPD. In clinical samples of BPD patients screened for adult ADHD, the prevalence of adult ADHD is higher than in the general population, ranging from 16.1% to 38.1%; 4,8,30-32 notably, women with ADHD, especially the combined type, have been reported to be more likely to have BPD than men with ADHD, whom more likely present with antisocial personality disorder.<sup>33</sup> In forensic settings, Rösler et al<sup>34</sup> found that female offenders with ADHD had BPD (63.6%) more often than offenders without ADHD (25.3%). Regarding population samples, results from the National Epidemiologic Survey on Alcohol and Related Conditions found that lifetime comorbidity in adults with BPD in the ADHD population was 33.7% compared with a lower prevalence of BPD of 5.2% in the general population.<sup>3</sup>

Altogether, a number of studies point to the fact that ADHD symptoms assessed retrospectively in patients with BPD occur more often than expected by chance and the co-occurrence of adult ADHD and BPD reported in several settings is high. Few studies have attempted to assess the co-occurrence between the disorders longitudinally, and found that childhood ADHD symptoms are significantly associated with an increased likelihood of BPD diagnosis in adulthood. <sup>28,29,35</sup>

# Psychopathological, Neuropsychological And Brain Mechanisms

In order to improve the understanding between the cooccurrence of BPD and ADHD, a critical issue is the symptomatic overlap between the BPD and ADHD regarding two key clinical dimensions, ie, impulsivity and emotional dysregulation<sup>36</sup> but also low self-esteem and disturbed interpersonal relationships which are common in both disorders.<sup>18</sup>

In one of the first studies investigating the specificity of the overall ADHD clinical dimensions in ADHD compared to BPD, Dowson et al<sup>36</sup> found, using a self-report measure, that inattention, lack of organization and persistence differentiated ADHD from BPD alone, whereas interpersonal impairment did not. These results led the authors to conclude that their self-report scale was valid, as it assessed symptoms specifically found in ADHD. In two more recent studies however, Edebol et al<sup>37</sup> and Weibel et al<sup>31</sup> assessed the psychometric properties of the World Health Organization Adult ADHD Self-Report Scale v1.1 (ASRS-v1.1) and found that it lacked clinical specificity in adult ADHD (i.e., its ability to discriminate BPD alone from BPD+ADHD), a finding that was likely due to shared symptoms of emotion dysregulation and impulsivity.<sup>31</sup> In addition, inattention may also be experienced in BPD, albeit in a special form as part of dissociative states, hence diminishing its power to discriminate the two disorders at least through self-report scales<sup>32</sup>

Somewhat similar results were found in a study by Philipsen et al<sup>38</sup> when BPD symptoms were assessed in adult patients with ADHD using the Borderline Symptom List (BSL)<sup>39</sup> Overall, lower scores were found in patients with ADHD compared to BPD patients, but scores in ADHD were higher on all subscales compared to healthy controls. Interestingly, particularly with respect to self-destruction and affect dysregulation, borderline symptoms in adult ADHD seemed to be less pronounced than in patients with BPD.<sup>38</sup>

### **Impulsivity**

Impulsivity has been identified as one of the dimensions having the greatest overlap between ADHD and BPD in adults<sup>40</sup> Both ADHD and BPD report higher levels of traitimpulsivity compared to healthy controls when using self-report measures such as the Barratt Impulsiveness Scale (BIS).<sup>26,41</sup> Adults with ADHD+BPD and ADHD alone report however a higher level of trait-impulsivity compared to BPD alone<sup>12,26,42–44</sup> and such is also the case for informant-rated impulsivity in ADHD+BPD compared to ADHD alone<sup>40</sup> Impulsivity is a multi-faceted concept, and divergent findings have been reported across studies in terms of which dimensions show greater impairment in the three groups of patients. For instance, using the BIS, both

Prada et al<sup>4</sup> and Lampe et al<sup>44</sup> found that motor impulsivity best distinguished ADHD and BPD+ADHD subjects from BPD alone, with the highest scores found in ADHD and BPD+ADHD. By contrast, Speranza et al<sup>26</sup> showed, using the same scale, that higher levels of Attentional/Cognitive trait-impulsivity were particularly associated with ADHD diagnosis in BPD adolescents. Using a self-report measure, Dijk et al<sup>45</sup> showed that high Novelty Seeking, which is related to impulsivity, was more strongly linked to ADHD than to BPD.

From a neuropsychological standpoint, impulsivity is assessed using a wide range of tasks targeting specific aspects of behavior control. 46 Compared to healthy controls, adults with ADHD display impairment in most response inhibition paradigm studies<sup>47</sup> whereas more conflicting findings have been reported in BPD, where inhibition impairment has been found mainly in emotionally conditioned tasks. 48,49 Specifically, most studies have found delay discounting deficits in adults with BPD;<sup>50,51</sup> however, only some studies have observed impaired response inhibition in BPD patients compared to healthy participants, 52,53 while others have not found significant differences. 54,55 Few studies have compared cognitive inhibition performance in BPD, adult ADHD, and BPD+ADHD groups, and most have reported greater impairment in ADHD and ADHD+BPD compared to BPD alone (with one exception)<sup>56</sup> In a first study, Nigg et al<sup>57</sup> compared the performance of 105 adults with ADHD (of whom 20% with co-occurring BPD) and 90 healthy controls in the stop signal task, and found that response inhibition deficits were correlated to BPD symptoms. However, when ADHD symptoms were entered as a predictor, response inhibition ceased to be significantly associated with BPD symptoms. In another study, Lampe et al<sup>44</sup> found that adults with ADHD performed worse than BPD individuals and healthy controls in two cognitive inhibition control tasks, while non-comorbid BPD subjects did not differ from their matched controls, suggesting that impaired inhibitory control is found in BPD+ADHD but not in BPD alone. In another study, O'Malley et al<sup>40</sup> found greater attention and working memory impairment in adults with ADHD+BPD compared to non-comorbid ADHD, whereas inhibition of prepotent responses did not differ between groups, hence suggesting that the comorbid group presented with more severe cognitive impairment. Finally, in a series of studies, Krause-Utz et al<sup>46</sup> Cackowski et al<sup>58</sup> and Krause-Utz et al<sup>43</sup> investigated the role of stress in different components of impulsivity in BPD compared to adult ADHD. In a first study, Krause-Utz et al<sup>46</sup> proposed the Go/NoGo task before and after moderate stress induction in female adults with BPD alone, ADHD alone, BPD+ADHD, and female healthy controls. While ADHD and BPD+ADHD showed significantly more errors under stressful and non-stressful conditions, BPD did not differ from healthy controls. In a follow-up study by Cackowski et al<sup>58</sup> BPD patients showed significantly impaired performance on a Stop-Signal task after severe stress induction, when including ADHD symptoms as a covariate. Krause-Utz et al<sup>43</sup> replicated and expanded on these findings as they showed that, under severe stress only, BPD patients performed significantly worse than healthy controls, while ADHD showed significant action-withholding deficits under stressful and non-stressful conditions.

Functional neuroimaging data of frontal dysfunction of inhibitory control in BPD and ADHD are mostly consistent with the aforementioned behavioral results<sup>48</sup> Indeed, overall, patients with BPD exhibit prefrontal dysfunctions in orbitofrontal, dorsomedial, and dorsolateral prefrontal regions when they perform impulse control tasks, whereas adults with ADHD display disturbed activity mainly in ventrolateral and medial prefrontal regions. This suggests a dissociation of frontal dysfunctions in BPD and ADHD, although only few studies have provided a direct comparison of these disorders and assessed different facets of inhibition control.<sup>48</sup>

Comparative data on impulsivity is scarce in ADHD, BPD, and BPD+ADHD. Nevertheless, the available results point to two directions: first, there might be a subgroup of individuals with BPD with high levels of trait-impulsivity, and those individuals seem to correspond to the comorbid BPD+ADHD type; 4,12,26,40 second, unlike ADHD, impulsivity in BPD might be intrinsically related to emotion dysregulation, that is, in highly stressful conditions, individuals with BPD exhibit more pronounced impulsive behaviors whereas in ADHD impulsive behaviors seem to be less stress-dependent. 59

## **Emotion Dysregulation**

Emotion dysregulation is a core mechanism of BPD concerning at least two of the DSM-5 criteria for the disorder<sup>1</sup> In terms of the dynamics of emotion dysregulation in BPD, a recent review of 34 studies using ecological momentary assessments found that BPD patients experience longer duration of aversive tension and a slower return to their baseline affective state<sup>60</sup> Relative to BPD, in ADHD, emotion dysregulation has been understudied until recently, although it is a frequent symptom that is associated with poorer functioning outcomes, regardless of

other psychiatric comorbidities. 5,60-64 Research has shown that emotion dysregulation in ADHD is similar to that found in BPD, including increased instability and intensity of negative emotions and a slow return to emotional baseline when activated. 62,64 However, to our knowledge, only three studies have directly compared emotion dysregulation in ADHD, BPD, and BPD+ADHD, with conflicting results. Cavelti et al<sup>65</sup> compared self-assessed trait emotion regulation skills in 80 adults with ADHD, 55 with BPD, and 55 healthy participants. The authors found no differences between the clinical groups on self-reported emotion regulation skills which were significantly worse than those reported by healthy controls. In another study, Cackowski et al66 found that adult ADHD and BPD patients scored significantly higher on all self-report measures of trait anger, anger expression, aggressive and antisocial behavior compared to healthy controls. Compared to ADHD patients, BPD patients reported higher trait aggression and hostility, as well as a stronger tendency to express anger when provoked, and to direct anger inwardly. Furthermore, after stress induction, BPD patients exhibited higher state anger than healthy controls and ADHD patients. Of particular interest, BPD patients reported more severe trait emotion dysregulation on the Difficulties in Emotion Regulation Scale (DERS)<sup>67</sup> compared to healthy controls and ADHD patients, and emotion dysregulation was significantly associated with elevated self-reported proneness to anger and aggression. In a recent study, Rüfenacht et al<sup>60</sup> found that adults with ADHD had significantly better self-reported emotion regulation strategies than patients with BPD alone, and BPD +ADHD. Specifically, adults with ADHD showed lower emotional reactivity, better use of adaptive cognitive strategies and lesser use of non-adaptive strategies compared to the two other groups.

Overall, trait emotion dysregulation is clearly overrepresented in ADHD compared to healthy controls, and it has been argued that it could be a key feature of the disorder<sup>68</sup> Like BPD, ADHD is a heterogeneous disorder, and it is likely that subgroups differ in terms of executive dysfunction<sup>69</sup> but also of emotion regulation deficits<sup>70</sup> Consistent with this hypothesis, Hirsch et al<sup>70</sup> recently found that empirically derived symptom profiles revealed two clusters of adult patients with ADHD: the first comprised substantial proportions of the inattentive and the combined subtype, and the second included patients with severe emotion dysregulation, higher psychosocial impairments, and more comorbidities, including personality disorders.

The neuropsychological underpinnings of emotion regulation deficits in ADHD and BPD are still mostly unknown<sup>71</sup> In ADHD, there are two main hypotheses: the "dyscontrol hypothesis" whereby emotion dysregulation is driven by the same cognitive and neural processes that drive ADHD, mainly deficits in top-down executive control; and the "affectivity hypothesis" that states that emotion dysregulation is related specifically to emotional regulation neural processes, separate from those that lead to ADHD symptoms<sup>72</sup> To date the accumulating evidence is pointing to the affectivity hypothesis<sup>71</sup> Regarding BPD, a critical review of fMRI studies concluded that emotion dysregulation was associated with increased amygdala activity and decreased activity within prefrontal regions, suggesting an impaired fronto-limbic inhibitory network<sup>73</sup> In a recent review, Petrovic & Castellanos<sup>74</sup> proposed that the difference between ADHD and predominantly emotional instability disorders such as BPD is whether there is a dysfunctional top-down regulation of non-emotional (and exteroceptively associated) processing or emotional (and interoceptively associated) processing subtended respectively by (i) the rostral ACC and the lateral orbitofrontal cortex and (ii) the caudal anterior cingulate cortex (ACC) and the and dorsolateral prefrontal cortex. In this sense, they speculated that ADHD patients presenting with emotion dysregulation symptoms would have poor capacity for both non-emotional and emotional regulatory processing. A putative extreme situation of very low emotional regulatory processing associated with low nonemotional processing would lead to the comorbid BPD +ADHD. In this somehow dynamic perspective, Petrovic & Castellanos<sup>74</sup> proposed to view both disorders in a dimensional fashion as these neural systems are highly interdependent, and possibly modulated by the dopaminergic system.<sup>74</sup>

### Interpersonal Problems

Interpersonal problems are often found in both BPD and ADHD, <sup>4,36</sup> and are related to decreased quality of life and self-esteem found in both disorders. <sup>40,75–77</sup> In BPD, interpersonal difficulties are a cardinal symptom of the disorder, defined by unstable and intense relationships with an alternation between idealization and devaluation, as well as high interpersonal sensitivity and efforts to avoid abandonment. <sup>1,77</sup> In ADHD, interpersonal problems have been conceptualized as being consecutive to its core triad of symptoms inattention,

impulsivity and hyperactivity as well as social cognition deficits, all of which might be interpreted in the context of frontostriatal dysfunction<sup>78</sup> A number of studies have shown that interpersonal difficulties in BPD are related to both emotion dysregulation and impulsivity, but also to mentalizing abnormalities, that is, the ability to comprehend one's own and others' behavior in terms of intentional mental states<sup>77</sup> For instance, Herr et al<sup>79</sup> found that the association between overall BPD symptomatology and interpersonal problems was fully mediated by emotion regulation deficits. More recently, emotion dysregulation and attentional impulsiveness were shown to predict interpersonal problems directly in adult BPD subjects, whereas hypomentalizing predicted interpersonal problems indirectly throughout emotion dysregulation and attentional impulsiveness<sup>77</sup> These results hence suggested that targeting emotion dysregulation, impulsivity, and mentalization might impact interpersonal problems in BPD. In adult ADHD, the mechanisms involved in interpersonal problems have been less studied. 78,80 Although young adults with ADHD report having higher levels of interpersonal problems relative to healthy controls, they tend to underreport hostile interpersonal problems<sup>82</sup> probably due to mentalization deficit and reduced empathy. 61,80 To our knowledge, only two studies have directly compared adult ADHD, BPD, and BPD+ADHD on mentalization and empathy skills. In a first study, participants with ADHD showed self-reported mentalization scores mid-point between healthy controls and participants with BPD. Interestingly, those with comorbid BPD+ADHD achieved the lowest mentalization scores of all groups, and the severity of ADHD symptoms was correlated with poorer mentalization levels in all clinical groups<sup>80</sup> In another recent study, Rüfenacht et al<sup>61</sup> found that ADHD as well as BPD subjects displayed lower self-reported empathy than a sample of healthy subjects, a finding interpreted as being related in both cases to emotion dysregulation and mentalizing difficulties. The authors thus speculated that targeting protective mentalization and emotion dysregulation early in development may help prevent the persistence of ADHD into adulthood and the emergence of comorbid mood and personality disorders.<sup>61</sup>

# **Etiological Factors**

Early theoretical models of BPD emphasized the role played by childhood sexual abuse as a major risk (and etiological) factor for BPD<sup>81</sup> It has since been recognized that severe abuse occurs only in a minority of BPD patients, with a small effect size<sup>82</sup> and that childhood maltreatment is a non-specific risk factor for a diverse range of disorders<sup>83</sup> Such is the case for adult ADHD, where childhood

emotional abuse and neglect are more commonly reported relative to healthy controls<sup>84</sup> Most evidence now supports gene–environment interaction and correlation in the development of both BPD and ADHD, <sup>85,86</sup> with different heritability rates for each disorder. <sup>87,88</sup> This means that individuals with a "sensitive" genotype are at greater risk in the presence of a predisposing environment.

### Genetic Studies

While it is firmly established that genetic factors play a central role in the etiology of ADHD, with heritability estimates ranging between 70-80%87 the literature in BPD remains relatively underdeveloped in this field. Familial and twin studies indicate a genetic component to adult BPD, with heritability estimates ranging from 35% to 46% 88-90 although no gene has been identified to date. 88,89 Only two studies have investigated the shared genetic and environmental contributions to ADHD and BPD. In a first study, Distel et al<sup>86</sup> investigated ADHD and borderline symptoms in a sample of 7,233 twins and siblings in the Netherlands; results showed that half of the association between ADHD and BPD was explained by genetic factors, while the remaining part of the association was due to environmental factors unique to the individual. Recently, Kuja-Halkola et al<sup>90</sup> explored familial co-aggregation of clinically diagnosed ADHD and BPD from a sample of 2,113,902 individuals registered in a cohort study in Sweden. The authors found that individuals with a diagnosis of ADHD had 19.4 times higher odds of BPD diagnosis than individuals not diagnosed with ADHD. Moreover, the pattern of familial co-aggregation of ADHD and BPD across different types of relatives indicated that genetic factors were involved in ADHD and BPD co-occurrence. Interestingly, Mistry et al<sup>91</sup> recently reported that polygenic risk score for bipolar disorder was strongly linked to childhood ADHD, but not to BPD traits, suggesting different genetic background for ADHD and BPD.

# Developmental Pathways And The Role Of Temperament And Traumatic Events Early- Or Late-Onset Disorders?

The most supported pathogenesis theory of BPD is the one proposed by Linehan<sup>15</sup> which suggests that BPD results from the interactions between biological and psychosocial factors<sup>81</sup> in particular between biologically based temperamental vulnerabilities and adverse and traumatic experiences during childhood. Age of onset of BPD is a controversial topic, but

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most research now considers that BPD diagnosis may be established in adolescence, 26,92 and symptoms by the age of 12 predict psychosocial functioning during the transition to adulthood<sup>92</sup> This highlights the genetic component involved in the pathogenesis of BPD, which had been overshadowed by earlier models that focused solely on environmental risk factors for the disorder. 81,92 From a lifespan perspective, there is evidence that the prevalence of BPD symptomology decreases with age<sup>93,94</sup> and that older adults are less likely than younger adults to endorse specific BPD symptoms such as impulsivity, self-harm/suicidality and affective and interpersonal instability<sup>95</sup> By contrast, ADHD is usually viewed as a neurodevelopmental disorder: symptoms must be present before the age of 12<sup>1</sup> and are mostly stable across time, though some decline in adulthood has been reported<sup>96</sup> Recently however, the neurodevelopmental basis of ADHD has been called into question, as in three birth cohorts followed up until adulthood, a vast majority of those with adult ADHD did not have significant ADHD symptoms during childhood, and the overlap between ADHD diagnosed in childhood and ADHD diagnosed in adults was low. 97-99 Thus, these results indicate that either adult-onset ADHD is a distinct clinical entity 100 or the developmental pathways involved in early- and late-onset ADHD differ while sharing the same genetic, environmental and underlying neural mechanisms, due to fluctuating environment pressure or preventive factors<sup>101</sup> Importantly, it is still unknown whether age of onset of symptoms is involved in the likelihood of presenting with the comorbid ADHD+BPD clinical picture in adulthood. Van Dijk et al<sup>102</sup> showed, using latent class analyses, that some cases of comorbid ADHD+BPD symptoms in adults were not preceded by significant childhood ADHD symptoms, consistent with the late-onset ADHD construct. However, predominant BPD symptoms could be traced back to ADHD symptoms in childhood, especially hyperactivity/impulsivity symptoms. The authors thus concluded that there were two possible developmental pathways: the first leading from combined ADHD symptoms in childhood to adult ADHD, and the second leading from childhood hyperactive/impulsive symptoms to an adult profile of ADHD +BPD symptoms.

### **Temperament**

Temperament has been conceptualized as a genetically influenced building block of personality; it has been shown to be highly heritable and relatively stable across the lifespan<sup>103</sup> ADHD and BPD share a number of temperament traits, especially novelty seeking and harm avoidance<sup>104</sup> Novelty seeking, a construct closely related

to impulsiveness, has been associated with BPD<sup>105</sup> in male patients in particular whereas harm avoidance has been reported in female patients with BPD<sup>106</sup> Similarly, in ADHD, novelty seeking has been found to predict ADHD diagnosis<sup>103</sup> and increased harm avoidance has also been reported in ADHD104 In a recent systematic review on temperament correlates in adult ADHD, Pinzone et al<sup>107</sup> found high scores on the Novelty Seeking and Harm Avoidance subscales and low scores on the Persistence subscale of the Temperament and Character Inventory (TCI)<sup>108</sup> compared to healthy controls. Using the Temperament Evaluation of Memphis, Paris and San Diego-Auto-questionnaire (TEMPS-A)<sup>109</sup> which assesses affective temperaments derived from a kraepelinian framework, the authors found that the majority of ADHD individuals shared temperament traits such as cyclothymia and irritability with patients with bipolar disorder, but not hyperthymia. Importantly, both BPD and ADHD disorders are highly comorbid with bipolar disorder, 110,111 a finding that has raised the question of whether this overlap is also found at the temperament level<sup>111</sup> Although it is beyond the scope of this review to include findings relative to bipolar disorder, it is noteworthy that similar cyclothymic temperament traits levels, which are related to affective instability, have been reported in BPD, ADHD and bipolar disorder, suggesting that affective instability is a core temperament dimension shared by the three<sup>111</sup> Few other studies have directly compared temperament traits in BPD, adult ADHD, and BPD+ADHD. In one of them, van Dijk et al<sup>45</sup> found that high Novelty Seeking was particularly associated with inattention symptoms of ADHD, and the highest Novelty Seeking temperament scores were found in ADHD+BPD. By contrast, high Harm Avoidance, low Cooperativeness, and low Self-directedness were specifically related to BPD symptoms. In another study, Carlotta et al<sup>112</sup> found that action-oriented features - ie, impulsivity, aggression, novelty seeking, and juvenile conduct problems - completely mediated the relationship between retrospective ADHD symptoms and current BPD features, suggesting that impulsivity might be particularly involved in the cooccurrence of BPD and ADHD.

### Adverse And Traumatic Experiences

The most supported theory of BPD posits that the disorder occurs in the context of an interaction between temperamental traits, especially impulsivity and emotion dysregulation, and an invalidating childhood environment

characterized by intolerance toward the expression of private emotional experiences<sup>15</sup> Children exposed to such adverse environments are therefore unable to learn how to effectively regulate their emotions, and they vacillate between emotional inhibition and extreme emotional lability<sup>15</sup> Several studies have shown that BPD is associated with childhood abuse and neglect more than any other personality disorder. 93,113 and emotion regulation difficulties have been shown to be key mediators in the relationship between childhood trauma and BPD<sup>114</sup> As outlined above however, adverse and traumatic events are very prevalent in personality disorders as a whole 115 but also in ADHD as well as in other psychiatric disorders 116 For instance, a recent cohort study in Sweden found an increased risk for ADHD (OR 5.5, 95% CI 5.0-6.0) in individuals who had been repeatedly exposed to childhood adversity<sup>116</sup> Given this, a critical issue is whether the same type of adverse and traumatic events is involved in the pathogenesis of BPD, ADHD, and BPD+ADHD. In one of the first studies investigating this topic, Philipsen et al<sup>8</sup> found higher rates of emotional abuse in BPD females with childhood ADHD symptomatology compared to those who had few childhood ADHD symptoms, and this was associated in turn with more severe borderline symptomatology in adulthood. Sexual and physical abuse did not distinguish the two groups of BPD patients. Recently, Ferrer et al<sup>117</sup> reported that physical abuse in childhood was associated with the persistence of ADHD into adulthood, while emotional or sexual abuse was predictive of development of BPD or comorbid BPD+ADHD, hence highlighting that specific traumatic events could increase the likelihood of developing either ADHD alone or BPD and BPD+ADHD. In another recent study, Richard-Lepouriel et al<sup>42</sup> compared self-reported childhood traumatic events in BPD, adult ADHD, bipolar disorder and healthy adults. Relative to adult ADHD, BPD patients had higher scores for emotional and sexual abuse; for sexual abuse in particular, BPD patients had higher scores than any another population. Scores were higher in ADHD compared to healthy controls in all subscales of the Childhood Trauma Questionnaire (CTO)<sup>118</sup> except for sexual abuse, while relative to bipolar disorder, adults with ADHD showed higher scores for emotional and physical abuse, but also physical neglect. Of note, female gender has been reported to predict the developmental progression of childhood ADHD to adult BPD<sup>119</sup> a finding that may be due to the fact that sexual abuse in childhood is more prevalent among women, on the one hand, and that sexual abuse is a vulnerability risk for BPD<sup>119</sup> One possibility is that, in genetically susceptible individuals, early-life exposure to adversity may alter trajectories of brain development and increase the vulnerability to psychopathology. Severe childhood maltreatment, especially sexual abuse, is thought to be involved in the precursors of borderline symptoms through its impact on hippocampal volume, amygdala reactivity, and the development of frontal lobe functions in particular, which is involved in self-control and emotion regulation. 120,121 It has been argued that during early childhood the prefrontal cortex forms the basic neural circuitry (through synaptic production) that is modified in adolescence (synaptic pruning)<sup>122</sup> Since the prefrontal cortex subtends attention control abilities, it is unsurprising that maltreated children will be more likely to present attention and executive dysfunction, consistent with a diagnosis of ADHD<sup>122</sup> It is still unknown however whether the phenomenology of attention and executive dysfunction in these individuals differs from those who present with ADHD and fewer childhood adversity events. We speculate that emotional and sexual childhood abuse in particular might be involved in the emergence of symptoms of BPD, such as dissociative states and emotion dysregulation.

In addition to different types of adversity, timing of exposure during different developmental periods could be an important factor for differential disease risk<sup>123</sup> and could be mediated by differential vulnerability of certain systems during developmental periods<sup>124</sup> This means that investigating the differential disease risk relative to type of adversity, but also timing of exposure in BPD, ADHD, and BPD+ADHD could be particularly relevant to the understanding of their specific developmental pathways.

Given the increasing evidence supporting the role played by adverse and traumatic events on the emergence of psychopathology<sup>124</sup> there has been a shift in ongoing research in psychiatric disorders from identifying "vulnerability genes" to identifying genes that can be influenced by the environment and contribute to adult psychopathology<sup>125</sup> Epigenetics, which refer to the study of modifications of gene expression rather than alteration of the genetic code itself, has been investigated in relation to childhood adversities mainly in BPD. Genes involved in the regulation of the hypothalamic–pituitary–adrenal (HPA) axis have shown promising results<sup>126</sup> However few studies have investigated this issue in ADHD and few epigenetic changes in relation to early life adversities have been shown to be shared between ADHD and BPD. <sup>125</sup>

### **Discussion**

Over the last decades, interest in the relationship between ADHD and BPD has increased, owing to the growing number of studies that have reported high rates of comorbid BPD+ADHD, and the poorer functioning found in the comorbid form<sup>4</sup> Four possible explanations as to why the two disorders frequently co-occur have been put forward: i) ADHD may be a developmental precursor of BPD; ii) BPD and ADHD may correspond to different expressions of the same disorder rather than two distinct clinical entities; iii) ADHD and BPD may be distinct disorders sharing common etiological risk factors; and iv) the presence of one disorder may increase the risk of developing the other. 4,16 The phenotypic overlap between the two disorders, as well as the high rates of co-occurrence and familial aggregation, support the role played by shared risk factors. 90,112 This points to the fact that symptoms should be considered dimensionally and an important focus should be put on the developmental pathways involved in their emergence and persistence. Importantly, the boundaries between BPD and ADHD have become less clear over the last two decades, with research showing that adverse childhood events might increase the risk of developing ADHD. 84,116 and that borderline symptoms predictive of adult BPD diagnosis can be traced back to childhood.<sup>92</sup> This highlights the need for more research into the developmental pathways involved in the emergence of both disorders. Traditionally, BPD and ADHD were conceptualized as either a late-onset and traumarelated disorder (for BPD) or an early-onset neurodevelopmental disorder (for ADHD). Our review highlights the recent shift toward a diathesis biopsychosocial model whereby both biological and environmental factors are involved in the pathogenesis of BPD and ADHD. This bears some important clinical and research implications as there are probably neurodevelopmental aspects involved in the emergence of BPD, and there are environmental aspects involved in the emergence and/or the persistence of ADHD in adults.

Both in BPD and ADHD, phenotypic expressions are heterogeneous with some overlap between the two disorders at the dimensional level. The determinants of this heterogeneity are still largely unknown, making the available diagnostic categories imperfect. From a dimensional perspective, our review highlights that the co-occurrence between ADHD and BPD might be explained by two major shared dimensions – i.e., impulsivity and emotion

dysregulation – probably subtended by differential dysfunction of top-down regulation of emotional and non-emotional processing<sup>74</sup> Importantly, although impulsivity and emotion dysregulation are shared by ADHD and BPD, trait-impulsivity is higher in ADHD and ADHD+BPD compared to BPD alone, and trait-emotion dysregulation is higher in BPD and ADHD+BPD compared to ADHD, hence suggesting that in BPD impulsivity and emotion dysregulation are intrinsically related.<sup>58,74</sup> This means that, phenomenologically speaking, there might be differences in the way impulsivity and emotion dysregulation are expressed in BPD and ADHD alone; by focusing on these differences, clinicians might increase diagnostic specificity.

Historically, BPD has been considered as a psychological disorder whose first-line treatment is psychotherapy<sup>127</sup> Conversely, ADHD has been conceptualized as a neurodevelopmental disorder, whose treatment mainly relies on psychostimulant drugs<sup>32</sup> Both tend to be diagnosed and treated by specialists with expertise exclusively in one of the two disorders. Diagnosing adult ADHD might be difficult, especially when emotion dysregulation symptoms are present, and treatment of BPD patients requires well-trained therapists. Because of this, it is crucial that clinicians systematically inquire about the potential comorbidity. However, despite the importance of screening for ADHD in the context of BPD (and vice-versa), screening tools lack the ability to discriminate ADHD in BPD patients<sup>31</sup> and to our knowledge, the psychometric properties of BPD screening measures in adult ADHD have yet to be investigated. Therefore, clinicians should not rely on screening measures alone to make a diagnosis; instead, clinicians working in each field (BPD and ADHD) should be knowledgeable of the other field in order to effectively detect comorbid cases in clinical practice, based on the careful intake of the patient's psychiatric and developmental history.

Developmentally speaking, our review indicates that a subgroup of patients with childhood ADHD has relatively few emotion dysregulation symptoms, and they also have a lower risk of having a persistent ADHD clinical picture and developing BPD in adulthood. Another subgroup, probably characterized by higher levels of hyperactivity/impulsivity and emotional problems, seems more prone to develop the comorbid BPD+ADHD clinical presentation. It is unclear to what extent these clinical pictures are linked to either different neurobiological vulnerabilities, and/or their interaction with an unfavorable environment. Emerging evidence on the latter topic suggests that while

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childhood adversity may increase the risk of overall psychopathology<sup>124</sup> it is likely that repeated exposure to physical abuse in particular might be associated with the persistence of ADHD into adulthood, while emotional or sexual abuse might be particularly involved in the development of BPD or comorbid BPD+ADHD<sup>117</sup> Moreover, although still speculative, it is possible that ADHD symptoms in childhood, especially when untreated, may increase the odds of severe negative childhood experiences, and this, in turn, may predispose to the development of BPD in adulthood in a subgroup of individuals.<sup>8</sup>

Given that adult ADHD and BPD share a range of warning signs and risk factors, when focusing on the developmental pathways involved in the emergence of both disorders, it might be useful to consider ADHD and BPD dimensionally rather than as two categorical entities. Shared warning signs include impulsivity and anger, which have been found to be trait-like dimensions of BPD<sup>10</sup> as well as some of the main mediators of ADHD symptoms in childhood and BPD diagnosis in adulthood 112 In addition, emotion regulation difficulties have been shown to be key mediators in the relationship between childhood trauma and BPD<sup>114</sup> These results point to fact that if we are to design effective early preventive interventions in ADHD and BPD, those should be cross-diagnostic and based on clinical staging (ie, the severity and persistence of specific symptoms) instead of focusing on diagnostic categories and arbitrary age restrictions (i.e., early-onset for ADHD, and late-onset for BPD).<sup>10</sup>

In terms of treatment, there are several unmet needs that should be addressed. Treatment by psychostimulants in comorbid ADHD and BPD has only been tested in open trials<sup>128</sup> Furthermore, one non-randomized open study showed that psychostimulants improved response to psychotherapy in patients with the comorbid BPD+ADHD form<sup>129</sup> In ADHD alone, dialectical behavioral therapy (DBT) targeting emotion dysregulation has shown some encouraging effects in terms of global functioning. 130-132 Overall, despite the lack of robust evidence supporting the use of psychostimulants and psychotherapy in BPD +ADHD, this has been recommended by experts based on clinical experience<sup>32</sup> It is noteworthy that the moderating impact of the comorbidity has not been investigated in randomized controlled trial of psychotherapeutic treatments for BPD and pharmacological treatments for ADHD. Such studies are warranted in order to improve the understanding of how clinical heterogeneity, especially in terms of

Table I Keypoints And Suggested Directions For Research

- Adult ADHD and BPD are heterogeneous disorders that can no longer be viewed as purely early-onset neurodevelopmental (ADHD) or late-onset psychological disorders (BPD)
- Comorbid adult ADHD+BPD is frequent in clinical settings (16.1– 38% of BPD patients)
- The ADHD+BPD form is characterized by a more severe clinical presentation, i.e., higher trait-impulsiveness compared to BPD alone, and higher emotion dysregulation compared to ADHD alone
- Pathogenesis of ADHD and BPD involves some shared genetic, temperamental and environmental vulnerability factors, including childhood adversity
- Screening tools lack discriminative power in clinical settings, probably due to the shared symptomatic expressions between ADHD and BPD (e.g., emotion dysregulation and impulsiveness)
- Research is needed:
- To prospectively assess whether and how childhood ADHD symptoms increase the risk for BPD in adults
- To determine how the timing and the type of childhood adversity might differentially impact the development of ADHD, BPD, and ADHD+BPD in genetically susceptible individuals
- To identify children and adolescents at risk for the development of adult ADHD, BPD, and ADHD+BPD in order to design effective early interventions
- To assess the effectiveness of pharmacological and psychological interventions for comorbid cases

comorbid symptoms, impact treatment response. Main conclusions of the review are summarized in Table 1.

All in all, our study highlighted the overlap between BPD and ADHD, which is observed not only at the clinical level – that is, in terms of clinical expression, risk factors and particular developmental pathways – but also at the therapeutic level. This means that clinicians working with ADHD or BPD have to be particularly aware of their potential comorbidity and what it implies in terms of prognosis and treatment. Of particular clinical relevance, ADHD and BPD can no longer be viewed as either exclusively neurodevelopmental or psychological disorders. This has important clinical implications as preventive interventions should address trait-dimensions as well as environmental risk factors shared by ADHD and BPD in childhood, in order to improve the outcomes of individuals at risk.

### **Disclosure**

The authors report no conflicts of interest in this work.

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