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STUDY PROTOCOL

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Borderline personality disorder and post-traumatic stress disorder in adolescents: protocol for a comparative study of borderline personality disorder with and without comorbid post-traumatic stress disorder (BORDERSTRESS-ADO)

Maëlle Riou¹, Harmony Duclos⁴, Méline Leribillard¹, Jean-Jacques Parienti³, Shailendra Segobin¹, Armelle Viard¹, Gisèle Apter⁵, Priscille Gerardin^{6,7}, Bérengère Guillery¹ and Fabian Guénolé^{1,2*}

Abstract

Background Borderline Personality Disorder (BPD) is a prevalent and debilitating psychiatric condition often accompanied by Post-Traumatic Stress Disorder (PTSD), with a substantial prevalence of trauma history among affected individuals. The clinical, cognitive, and cerebral parallels shared with PTSD suggest a trauma-related etiology for BPD. Studies consistently demonstrate a reduction in hippocampal volume in individuals with BPD, echoing findings in PTSD. However, the interpretation of this shared neurobiological profile remains contentious, with ongoing debates regarding the independence of these pathologies or the potential exacerbation of diminished hippocampal volume in BPD due to concurrent PTSD. Differential impacts on hippocampal subfields across both disorders may further complicate interpretation, suggesting the volume of hippocampal subfields as a potential discriminant biomarker. This study aims to characterize the multidimensional specific and shared profiles of BPD and PTSD-related alterations, with a particular emphasis on hippocampal subfields during adolescence, a crucial period in BPD development.

Methods This study focuses on female adolescents, who are more prevalent in the BPD population. Participants are categorized into three groups: BPD, BPD with comorbid PTSD, and a control group of matched healthy individuals. Data collection encompasses clinical, cognitive, and neuroimaging domains commonly affected in both disorders, utilizing various imaging markers (including gray matter macrostructure, white matter microstructural integrity, and regional functional connectivity).

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Discussion This study examines adolescent BPD with and without comorbid PTSD on clinical, neuroimaging, and cognitive levels. It is the first to use a comprehensive multi-modal approach within the same sample. Additionally, it uniquely explores hippocampal subfield volume differences in adolescents. Analysis of the relationship between the investigated domains and the effects of PTSD comorbidity will elucidate specific and shared alteration profiles in both disorders.

Trial registration IDRCB number 2019-A00366-51 / clinicaltrials.gov ID: NCT0485274. Registered on 21/04/2021.

Keywords Adolescent, Female, Post-traumatic stress disorder, Neuroanatomy, Borderline personality disorder, Comorbidity, Psychopathology, Emotional regulation, Hippocampus

Introduction

Borderline personality disorder (BPD) is a debilitating mental disorder, characterized by significant instability in affective, identity, and interpersonal functioning [1, 2]. More specifically, the core clinical features of BPD include emotional hyperreactivity, identity diffusion, and self-injurious behaviors [1, 3]. The lifetime prevalence of BPD is approximately 5% in the general population, with a sex ratio of 3 females to 1 male [4]. Patients with BPD represent 10 to 25% of patients in psychiatric clinics or hospitals, and globally display severe morbidity, poor functioning, and high mortality, primarily due to suicide [5]. The substantial individual and societal impact of BPD highlights its status as a major public health concern [2, 5].

The etiopathogenesis of BPD is complex, involving both genetic vulnerability and environmental factors. Among these, exposure to potentially traumagenic adverse life events in childhood stands out as one of the most significant factors [6]. This is reflected in the high comorbidity between BPD and post-traumatic stress disorder (PTSD), a trauma- and stressor-related disorder characterized by long-lasting symptoms such as psychic intrusions, avoidant behavior, and hyperarousal following exposure to a traumagenic event [3]. Concomitant PTSD is observed in up to 80% of BPD patients [7] and is associated with increased severity of BPD symptoms and reduced treatment efficacy [7, 8]. Moreover, patients with both BPD and PTSD experience more severe PTSD symptoms compared to those with PTSD alone [7].

Traumagenic events that have been prospectively associated with BPD mainly consist of childhood abuse, including emotional, physical, and sexual trauma [6], the same association being shown for childhood maltreatment as a whole [9, 10]. These findings highlight the developmental aspects of BPD, which show emotional and behavioral precursors in childhood [11, 12] and typically manifest during adolescence [1, 3]. Adolescence is indeed a critical period for the development and stabilization of emotional regulation [13], identity [14], and social cognitive functioning [15]. These developmental processes may be linked to the progressive maturation of

the prefrontal cortex during puberty and its interaction with limbic structures [16].

Limited knowledge exists regarding the brain underpinnings of BPD during adolescence. A few structural neuroimaging studies have indicated a reduction in gray matter volume (GMV) within the limbic cortical circuit [17–22] and the internal temporal lobe, including the hippocampus [23, 24]. In adults with BPD, structural studies have reported decreased GMV in fronto-limbic structures, such as the cingulate cortex, orbitofrontal cortex, prefrontal cortex, amygdala, and hippocampus [25]. Fewer studies have investigated the integrity of white matter (WM) tracts in BPD, with the most consistently observed findings showing decreased integrity of WM tracts in the corpus callosum and the hippocampal fornix [26].

These structural alterations closely resemble those observed in PTSD [27]. Notably, patients with PTSD exhibit decreased GMV within fronto-limbic structures [28, 29] and alterations in the integrity of WM tracts, including those in the corpus callosum and fronto-limbic fibers [28, 30]. Furthermore, resting-state fMRI studies in BPD have demonstrated disruptions in functional connectivity within the default mode network [25, 31], which aligns with patterns observed in PTSD patients [32].

Importantly, meta-analyses of brain structure in BPD underscores a reduction in hippocampal volume as a prominent finding [33–35]. This observation aligns with the critical role of the hippocampus within cortico-limbic circuits and some of the cognitive functions they're involved in, such as emotional regulation [36], impulsivity [37, 38], and higher-order cognitive dysfunctions, especially in memory functioning [39, 40].

Hippocampal volume and function also appear to be involved in the development and maintenance of PTSD symptoms [41]. Notably, reduced hippocampal volume is associated with an increased susceptibility to PTSD [42]. Conversely, heightened hippocampal activity has been linked to fewer PTSD symptomatology following exposure to potentially traumagenic events [43]. Moreover, a negative correlation between hippocampal volume and the severity of reexperiencing symptoms has been reported in PTSD patients [44].

The hippocampus has frequently been found to be involved in stress or -related psychopathology, mainly because of its sensitivity to biological stress [45, 46]. The glucocorticoid cascade hypothesis posits that persistent exposure to stress, such as childhood adversity, leads to a reduction in hippocampal volume through the cytotoxic impact of elevated cortisol levels [45–47]. This hypothesis has also been put forth as a neurobiological model for BPD [25].

The scientific literature exploring the role of PTSD on hippocampal alterations in patients with BPD is scarce and has yielded contrasting results. While some studies report that hippocampal GMV reduction in BPD patients is independent of PTSD comorbidity [34, 48–51], other ones suggest that decreased hippocampal volume in BPD may be amplified by, or even a consequence of, concurrent PTSD [52].

Specific profiles of GMV alterations in BPD and PTSD might be derived from the study of hippocampal subfields, allowing for more subtle analyses of volumetric differences. Interestingly, hippocampal GMV reduction in adolescents with PTSD has been shown to be driven by smaller volumes of some hippocampal substructures, the *Cornu Ammonis* (CA), specifically the CA2-CA3-Dentate Gyrus (DG) complex, which correlated negatively with the severity of reexperiencing symptoms [53]. Consequently, the volume of hippocampal subfields could be an interesting candidate as a predictive biomarker of PTSD outcome, as well as a biomarker of susceptibility to PTSD.

Hippocampal subfields have received very limited attention in BPD to date. A single study in BPD patients without comorbid PTSD has shown a reduction in volume in the stress-sensitive subfields DG-CA4 and CA2-3 compared to healthy controls. Interestingly, this volume loss exhibited no significant relationship with levels of childhood adversity [54]. Investigating the precise location of hippocampal volume loss might thus provide information on the differential role of the hippocampus in both BPD and PTSD psychopathology.

Methods

Aims and objectives

The BORDERSTRESS-ADO research project aims to comprehensively investigate the impact of chronic stress through the experience of adverse childhood events, with a specific focus on the influence of comorbid PTSD on the neurobiology and psychopathology of BPD. Notably, BPD typically emerges during adolescence, a critical period for its development, yet no such comparison has been conducted in adolescents to date. By identifying new markers associated with BPD, the outcomes of this study hold the potential to enhance the accuracy of BPD diagnosis in adolescents and will also provide evidence

to inform treatment decisions for this particularly severe condition.

Primary objective

The primary objective of this study is to investigate morphological modifications specific to PTSD in BPD population by comparing hippocampal volume in adolescents with BPD and those with comorbid BPD and PTSD. Each clinical group will first be compared to a healthy developing age-matched group.

Secondary objective

Primary analyses will be completed by comparisons of hippocampal subfields volumes across both clinical groups.

Exploratory objectives

Other secondary analyses will aim identifying specific and shared profiles of alterations between BPD and BPD with comorbid PTSD. Comparative and correlation analyses will be conducted on several measures, including WM microstructural integrity, resting-state functional connectivity (rsFC), and a range of cognitive and clinical variables of interest. Additionally, we aim to investigate the relationship between cerebral alterations and behavioral impairments in domains commonly affected in both BPD and PTSD. This will allow us to examine the impact of comorbid PTSD on the relationship between these variables and establish specific and shared profiles of multidimensional alterations in BPD and PTSD (see Fig. 1). This study will also assess the association between hippocampal volumes and the evolution of symptom profiles, employing a cross-sectional and repeated-measure design at 18 months post-inclusion.

Study design and overview

This study is a multi-center comparative study. We aim to recruit female adolescents from July 2022 to 2025 across 3 investigating centers (CHU Caen, CHU Rouen, GH Le Havre), 33 participants in each group (BPD, BPD/PTSD and healthy controls). Patients are pre-screened by a psychiatrist to check the inclusion criteria that are summarized in Table 1. Healthy controls interested in taking part in the study are pre-screened by a licensed psychologist during a telephonic interview. After providing an oral consent to participate, an interview is planned with the investigating psychiatrist, during which participants and their legal representatives are given the information notice, the consent forms and an answer to any question about the study. The inclusion visit (v0) is then scheduled after receiving informed written consent (see Fig. 2 for a depiction of participants' flowchart). This visit takes place in the inclusion site for patients, and in the research center for controls, and is divided into two parts. First, a

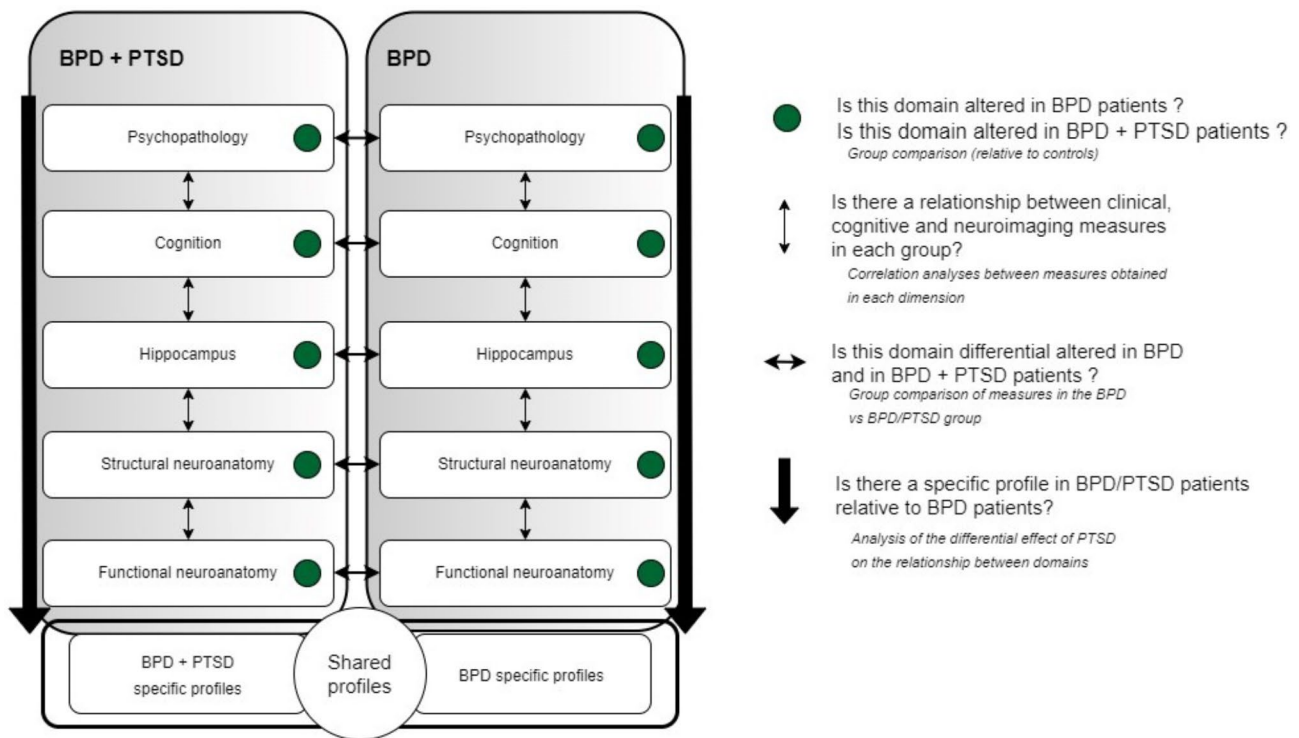


Fig. 1 Objectives of the BORDERSTRESS-ADO study. BPD: Borderline Personality Disorder, PTSD: Posttraumatic Stress Disorder

Table 1 Inclusion and non-inclusion criteria

	BPD	BPD/PTSD	HC
Inclusion criteria	<ul style="list-style-type: none"> • Female • 13–17 years old • Good understanding of written and spoken French • DSM-5 based diagnosis of BPD • Score > 20 CGA-S 	<ul style="list-style-type: none"> • Female • 13–17 years old • Good understanding of written and spoken French • DSM-5 based diagnosis of BPD • DSM-5 based diagnosis of PTSD • Score > 20 CGA-S 	<ul style="list-style-type: none"> • Female • 13–17 years old • Good understanding of written and spoken French • Absence of any mental disorders
Non-inclusion criteria	<ul style="list-style-type: none"> • Medicated attention deficit • Illiteracy • Presence of a major sensory disorder • Severe comorbid psychiatric disorder • History or presence of severe neurological disorder and/or alertness deficit • History of anoxic coma • Contraindication to MRI • Severe ongoing physiological disease • Inclusion in another biomedical research protocol during the study period • IQ < 70 		

BPD: Borderline Personality Disorder; PTSD: Post-traumatic stress disorder; HC: Healthy Controls; CGA-S: Clinical Global Assessment Scale

standardized psychopathological evaluation is conducted by a psychiatrist. Data obtained during this stage are used as objective arguments for group assignment during the team consensus best estimate diagnosis process (see measures and outcomes). The second part of the visit is conducted by a psychologist and aims to verify the cognitive inclusion criteria (Wechsler’s scales of intelligence). After this visit, two other ones are scheduled for neuropsychological assessments (v1(a)) and neuroimaging data collection (v1(b), Cycleron neuroimaging center, Caen). A

last visit after a period of 18 months is also planned for patients to conduct a clinical assessment (v2). Please see measures and outcomes for more details.

Study population

This study aims to compare female adolescents (N=99) with a diagnosis of BPD (N=33), a dual diagnosis of BPD and PTSD (N=33), and matched healthy controls (N=33). We decided to include only females to limit the

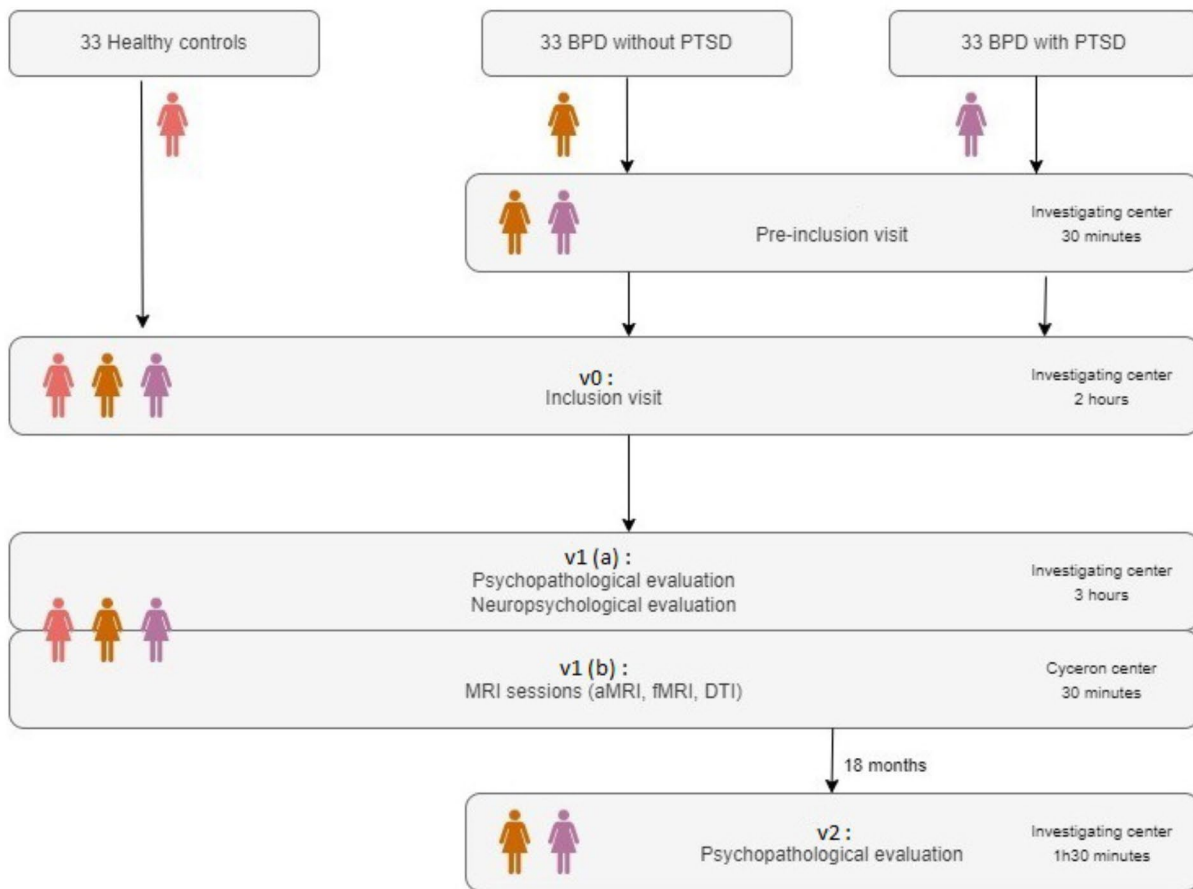


Fig. 2 Participants’ flowchart. There are three visits (v0, v1 and v2). The v1 visit is divided into two parts, v1 (a) at the Investigating center and v1 (b) at Cyceron center. BPD: Borderline Personality Disorder, PTSD: Posttraumatic Stress Disorder

heterogeneity in the population due to the sex ratio of 3 females for 1 male in the general population.

This sample size ($N=99$) was defined empirically, based on the recruitment capacity across the timespan of the study rather than based on a statistical hypothesis. Of note, the difference and standard deviation of hippocampal volume between groups, if any, are currently unknown. Nonetheless, the comparison of 33 subjects per group allows the detection of an anticipated effect size $ES=0.84$ (large), with a power of 0.915 and a two-tailed alpha risk of 0.05. This computation was performed with a software for a-priori Sample Size Calculator for Student t-Tests [55].

Patients are recruited in child and adolescent psychiatry department in the 3 investigating sites. Controls are recruited to match patients’ age, sociodemographic status, and education level by diffusion of flyers in schools and on social media. Patients planning to move to another region in the next 18 months following their inclusion are not included. Finally, patients with ongoing or past pharmacological treatment are not excluded, except in the case of a medicated attention deficit.

Treatment’s type and posology are registered and considered when analyzing neuroimaging data. The inclusion and exclusion criteria are further described in Table 1.

Measures and outcomes

Behavioral measures & analyses

Clinical evaluation: v0 The inclusion visit consists of a clinical evaluation to ensure the respect of inclusion and non-inclusion criteria, as well as to dispatch patients in the adequate group.

To determine group assignment (BPD vs. BPD/PTSD) for patients, the presence of PTSD is examined in a case conference using the team-consensus best estimate diagnoses method [56]. The decision is based on clinical data collected during the inclusion visit (T0), in the presence of the patient’s usual medical team. If the PTSD diagnosis is not confirmed in the case conference, the patient is assigned to the BPD group. Measures used for diagnosis and severity assessment are described in Table 2.

Table 2 Clinical assessments

Visit	Assessment	Test
v0	BPD diagnosis	SIDP-IV : Structured Interview for DSM-IV Personality [57]
Clinical evaluation	PTSD diagnosis	K-SADS-PL : Kiddie-Schedule for Affective Disorders and Schizophrenia [58]
	Severity of psychopathology	CGAS : Clinical Global Assessment Scale [59]
	Severity of PTSD symptoms	UCLA PTSD-RI C/A : Post-Traumatic Stress Disorder Reaction Index for Children and Adolescents [60]
	Presence of concomitant depression	ADRS : Adolescent Depression Rating Scale [61]
	Intensity of BPD symptoms	<i>Echelle de Traits de Personnalité Limite chez les Enfants</i> [62], BPFSC-11 : French version of the Borderline Feature Scale for Children [63]
	Intelligence	WISC-V : Weschler's Intelligence Scale for Children V [64] WAIS-IV : Weschler's Adult Intelligence Scale IV [65]
	Adverse life events	CTQ : Childhood Trauma Questionnaire [66, 67]

BPD: Borderline Personality Disorder; PTSD: Post-traumatic stress disorder

Table 3 Neuropsychological assessments

Visit	Assessment	Test
v1(a)	Insecurity of attachment	Ca-Mir : <i>Cartes des Modèles Individuels de Relations</i> [68]
Neuropsychological evaluation	Emotional Dysregulation	<i>Echelle Neuro-Affective de Personnalité</i> (French version of the Affective Neuroscience Personality Scale; ANPS) [69]
	Sustained attention	CPT : Continuous Performance Test [70]
	Executive functions	WSCT : Wisconsin Card Sorting Test [71]
	Social cognition: Theory of Mind	MASC : Movie Assessment of Social Cognition [72] RFQ : Reflective Functioning Questionnaire [73]
	Mental representations of self and others	AIDA : Assessment of Identity Development in Adolescence [74]
	Autobiographical memory	NaCCS : Narrative Coherence Coding Scheme [75]

Cognitive functioning: v1(a) All participants will undergo a set of neuropsychological evaluations, corresponding to affective and cognitive domains frequently altered in BPD and/or PTSD: emotional functioning, social cognition and more particularly theory of mind, identity diffusion and autobiographical memory and other associated abilities such as executive functions and quality of attachment (See Table 3 for details). All tests have shown good validity and reliability in adolescents.

Neuroimaging measures and analyses

Neuroimaging data will be collected using an MRI 3T Signa Premier General Electric Healthcare with a 48-channels head-coil, located in the Cyceron Center (Caen, France).

Structural MRI

Data collection Anatomical data will be collected using classical T1-weighted imaging on the whole brain. Volumetric T1-weighted images will be acquired at 1mm³ isotropic resolution to measure grey matter density and volumetry using a three-dimensional (3D) fast field echo sequence (sagittal acquisition; repetition time 2.2s; echo

time 2.7 ms; flip angle 8°; 180 slices; slice thickness 1 mm; matrix size, 256×256).

To investigate volumetric alterations specifically within the hippocampal subfields, a high-resolution two-dimensional T2-weighted image of the hippocampus will also be acquired (repetition time 8s; echo time 47 ms; flip angle 122°; 35 slices, slice thickness 2 mm; matrix size 448×448; in-plane resolution 0.4×0.4 mm²).

Data analysis Preprocessing of volumetric data will be done using SPM software (Statistical Parametric Mapping; Wellcome Department of Cognitive Neurology, London, UK), implemented in MATLAB (Mathworks Inc., Natick, MA). Obtained images will be normalized in a reference space based on the mean space from all the participants' data, using SPM's DARTEL.

Hippocampal subfields will be segmented with an automated method, developed in our research unit [53, 76]. This method is based on previous manual segmentation data and is comprised of a double random-blind measure regarding the participant's identity and clinical status. Whole brain voxel-based morphometry (VBM) analyses will be performed on MRI data using the SPM software. VBM analysis allows for a voxel-by-voxel group comparison of anatomical neuroimaging data.

Segmented hippocampal subfields will be used for group comparison of volume using Generalized Linear Models (GLM).

Resting state functional MRI (rs-fMRI)

Data collection Spontaneous cerebral activity will be measured through the temporal variations in BOLD's signal amplitude. The resting state BOLD signal will be obtained through a specific acquisition sequence (500 EPI volumes acquired with repetition time 1.2s; echo time 30ms; flip angle 66°; 60 slices with slice thickness 2.4 mm; matrix size 90×90; in-plane resolution 2.4mm²). Participants will lay down in the MRI machine, with the lights off, equipped with noise cancelling headphones. Instructions will be to avoid movement and speech, while letting their thoughts roam freely. A debriefing will take place after the MRI scanning session to evaluate participants' thoughts during the sequence. Additionally, physiological parameters known to affect the variations of the BOLD signal, such as respiratory and heart rate variations, will be collected throughout the acquisition. These parameters will be integrated in a model-based correction of physiological noise, which offers better denoising results than global signal removal [77].

Data analysis Preprocessing of resting-state fMRI (rsfMRI) data will consist in a volume-by-volume realignment and temporal interpolation of slices to correct for the temporal latency. rsfMRI measures spontaneous cerebral connectivity, which provides information on the way cerebral structures interact with each other at rest. Whole-brain connectivity analyses will be performed and used for group comparison.

Diffusion Tensor Imaging (DTI)

Data collection Diffusion data will be used to measure white matter microstructural integrity (A 2D-diffusion weighted sequence 64 directions; repetition time, 5.3s; echo time 73ms; flip angle 90°; slice thickness, 2 mm; matrix size, 108×108).

These data will be preprocessed to supply indirect measures of position, orientation, and anisotropy of white matter tracts. A reduction in anisotropy could reflect an alteration in density, diameter or thickness, or the thickness of the axonal myelin gains. Reconstructed DTI data will provide information on fractional anisotropy (FA) of white matter tracks and apparent diffusion coefficient (ADC). A reduced FA and/or ADC is thought to reflect a loss in white matter tracks integrity, possibly underlying impairments in cerebral connectivity.

Data analysis Preprocessing of DTI data will be done using FSL software (FMRIB Software Library v5.0, Oxford, UK) in order to produce eigenvalue and eigenvector images, which will be used to create fractional anisotropy maps, allowing tractography analyses (structural connectivity between preselected regions of interest, ROIs). Analyses of DTI data will be run in FSL, using the tract-based spatial statistics (TBSS) procedure, the equivalent of VBM for white matter analysis. This will permit group comparisons of the integrity of white matter tracks.

Statistical analyses

General outline Descriptive statistics of the participants will be computed through means (Standard deviation), medians (Interquartile range), or numbers (percentages), depending on whether the collected data are quantitative or qualitative.

All significance levels will be set at nominal p -value < 0.05, with two-sided hypothesis testing, due to the exploratory nature of this study, with no adjustment for multiple comparisons. Missing data are not expected but will be replaced using methods such as multiple imputations, assuming that the data will be missing at random [78].

Primary objective Linear regression analyses will be performed on whole hippocampal volume with clinical status as a predictor to investigate the volume differences between BPD, BPD/PTSD and healthy participants. Regression analyses will be adjusted for the effect of relevant demographic and cerebral parameters.

Secondary objective Segmented hippocampal subfields will be considered as ROIs and between-group volume differences will be assessed with linear regression with clinical status as a regressor. Regression analyses will be adjusted for the effect of relevant demographic and cerebral parameters.

Exploratory analyses Group comparison analyses for each domain will be performed first between each clinical group, i.e. BPD and BPD/PTSD, and the healthy control group using Student t -test or Wilcoxon sum-rank test in case of departure from the normal distribution. Second, comparisons will be performed between the two clinical groups. Then, within-group correlation using Spearman coefficient and least square linear regression analyses between measures obtained in each domain will be conducted to provide information on the relationship between clinical, cognitive and neuroimaging measures in each group. Finally, profile analyses will be conducted to determine the effect of an additional PTSD diagnosis on

the relationship between clinical, cognitive and neuroimaging measures (see Fig. 1).

To investigate the hypothesis that different clinical parameters and symptomatology affect different hippocampal subfields, regression analyses will be performed in each pathological group with hippocampal subfields as dependent variables and behavioral and clinical measures as regressors.

The putative role of the hippocampal volume as a predictor of the evolution of symptoms will be analyzed using repeated measures of clinical symptoms (baseline and 18 months). Repeated measures data will be analyzed with mixed models (Proc MIXED, SAS v9.4 software). The group will be set as fixed effect, and the intercept will be randomly defined to account for repeated measures across time. To test the role of the hippocampus on the evolution, mediation analyses on repeated clinical measures will be conducted with hippocampal volume as a mediator.

Discussion

This study aims to characterize adolescent BPD with or without comorbid PTSD on the clinical, neuroimaging and cognitive levels. Given the higher prevalence of BPD in females, our sample comprises female adolescents only to limit sex-related heterogeneity. To our knowledge, no previous study has compared adolescents with BPD to those with both BPD and PTSD. Furthermore, our study is the first to conduct a comprehensive assessment of psychological symptoms, cognition, and brain functioning in the same sample of adolescents with BPD adolescents, both with and without PTSD. Using multiple modalities within the same sample provides a unique opportunity to paint a more representative picture of the altered domains in BPD and PTSD, which is particularly important given the heterogeneous presentations of BPD. Notably, the volume of hippocampal subfields may be an interesting marker candidate differentiating between adolescents with BPD and those with both BPD and PTSD. A previous study conducted in our team indeed showed that hippocampal hypotrophies observed in youths with PTSD are driven by smaller volumes in specific hippocampal subfields [53]. Studying the precise location of hippocampal volume alterations in BPD may enhance our understanding of the specific brain changes associated with BPD in adolescence, while controlling for comorbid PTSD. Identifying specific and shared alterations in these populations could indeed be a stepping stone towards improving of the accuracy of BPD diagnosis in adolescents.

Abbreviations

ADC	Apparent Diffusion Coefficient
ADRS	Adolescent Depression Rating Scale
AIDA	Assessment of Identity Development in Adolescence

ANPS	Affective Neuroscience Personality Scale
BOLD	Blood-oxygen level dependent
BPFSC-11	Borderline Personality Features Scale for Children 11
BPD	Borderline Personality Disorder
CA	Cornu Ammonis
Ca-MIR	Cartes des Modèles Individuels de Relations (Maps of individual models of relationship)
CGA-S	Clinical Global Assessment Scale
CPT	Continuous Performance Test
CTQ	Childhood Trauma Questionnaire
DG	Dentate Gyrus
DTI	Diffusion Tensor Imaging
FA	Fractional anisotropy
fMRI	function Magnetic Resonance Imaging
GLM	General Linear Model
GMV	Grey Matter Volume
IQ	Intellectual Quotient
K-SADS-PL	Kiddie-Schedule for Affective Disorders and Schizophrenia
MASC	Movie Assessment of Social Cognition
MRI	Magnetic Resonance Imaging
NaCCS	Narrative Coherence Coding Scheme
PTSD	Posttraumatic Stress Disorder
RFQ	Reflective Functioning Questionnaire
ROIs	Regions of Interest
rsFC	Resting state Functional Connectivity
rs-fMRI	Resting state functional Magnetic Resonance Imaging
SIDP-IV	Structured Interview for DSM-IV Personality
SPM	Statistical and Parametrical Mapping
TBSS	Tract-Based Spatial Statistics
UCLA PTSD-RI C/A	University of California Los Angeles Posttraumatic Stress Disorder Reaction Index for Children and Adolescents
VBM	Voxel Based Morphometry
WAIS-IV	Weschler's Adult Intelligence Scale IV
WISC-V	Weschler's Intelligence Scale for Children V
WCST	Wisconsin Card Sorting Test

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Not applicable.

Author contributions

All authors were involved in developing the protocol and approved the final protocol manuscript. BGG, FG, and HD designed the study protocol. JJP substantially contributed to the statistical analyses plan. MR drafted the manuscript, and BGG, FG, JJP and SS revised it critically for important intellectual content. SS and AV substantially contributed to neuroimaging collection and analyses plan. ML contributed to neuropsychological data collection. FG, GA and PG coordinated patient inclusions. All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study follows the guidelines established in the French methodology of reference for studies in medical health (MR-001). Automated monitoring of health-related data is in line with the European Guidelines regarding the processing of personal data for scientific research purposes as established by the European Data Protection Board (April 27th, 2016). Clinical, neuropsychological, and socio-demographic data will be anonymized,

and each participant will be identified with a code. Imaging data will be anonymized according to the guidelines provided by the DICOM standard committee (Clinical Trials De-identification Profiles) and transmitted to the investigating team.

Explicit and informed consent from the participants and their legal representatives will be collected after they have been informed of the study objectives, its duration and procedure, as well as the potential risks and benefits of taking part in the research. Information notice will be given to both the participants and their legal representatives. Consent forms will be signed and dated by all involved parties, including a designated investigator. The medical procedures used in this study follow the guidelines of the Helsinki Declaration, as well as those of the law n°2012–300 (5th of march, 2012) and its application decree n° 2016–1537 (16th November 2016). Patients can retract their consent at any moment and can always exert their right to access and rectify their data. The promoter of the study will keep the participants informed of the results of the study at the end of the research.

An ID-RCB registration number has been requested from the *Agence Nationale de Sécurité du Médicament et des Produits de Santé* (ANSM): IDRCB number 2019-A00366-51. This study was approved by the *Comité de Protection des Personnes* (Ethics Committee) on 05 January 2021 (RI-HPS), after being registered as a clinical trial on clinicaltrials.gov (trial number: NCT0485274, registered on 21/04/2021).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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