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ABSTRACT

Stress reactivity is a complex phenomenon associated with multiple and multimodal expressions and functions. Herein, we hypothesized that compared with healthy controls (HCs), adolescents with borderline personality disorder (BPD) would exhibit a stronger response to stressors and a deficit in self-perception of stress due to their lack of insight.

Twenty adolescents with BPD and 20 matched HCs performed a socially evaluated mental arithmetic test to induce stress. We assessed self- and heteroperception using both human ratings and affective computing-based methods for the automatic extraction of 39 behavioral features (2D+3D video recording) and 62 physiological features (Nexus-10 recording). Predictions were made using machine learning. In addition, salivary cortisol was measured. Human ratings showed that adolescents with BPD experienced more stress than HCs. Human ratings and automated machine learning indicated opposite results regarding self- and heteroperceived stress in adolescents with BPD compared to HCs. Adolescents with BPD had higher levels of heteroperceived stress than self-perceived stress. Similarly, affective computing achieved better classification for heteroperceived stress. HCs had an opposite profile; they had higher levels of self-perceived stress, and affective computing reached a better classification for self-perceived stress. We conclude that adolescents with BPD are more sensitive to stress and show a lack of self-perception (or insight). In terms of clinical implications, our affective computing measures may help distinguish hetero- vs. self-perceptions of stress in natural settings and may offer external feedback during therapeutic interaction.

HIGHLIGHTS

- Affecting computing may help distinguishing heteroperceived stress from self-perceived stress
- Adolescents with BPD experience more stress than HCs during a socially evaluated mental arithmetic test
- Affective computing helped measuring BPD adolescents' lack of self-perception (or insight)

INTRODUCTION

Borderline personality disorder (BPD) is a severe and complex disorder characterized by fast and severe mood swings, out-of-control impulsivity, and self-harm behavior (e.g., self-cutting or suicide attempts) that primarily occurs in stressful contexts (Lieb et al., 2004; American Psychiatric Association., 2013). The prevalence of BPD is nearly 3% in adolescent general populations, 11% among psychiatric outpatients and up to 78% in suicidal adolescents attending an emergency department (Guilé et al., 2018). The burden of the disorder is also related to the high prevalence of patients who die by suicide: up to 10% of BPD patients die by suicide, which is almost 50 times higher than the rate in the general population (Lieb et al., 2004).

The relevance of the diagnosis of BPD in adolescents has been debated. The personality is still under construction at this age, and, in diagnostic and statistical manual of mental disorders, a diagnosis of BPD (or a diagnosis of any other personality disorder) should be restricted to patients over 18 years old. However, numerous clinicians have stressed that (1) BPD usually begins in adolescence; (2) from a symptomatic and therapeutic point of view, a diagnosis of BPD may be relevant in adolescents, (3) its use would crucially allow the adolescent to begin specific treatment; and (4) treatment options are much the same as in young adults (Paris, 2004; Chaney et al., 2020). Thus, without considering BPD as a structural and fixed pattern in young individuals, BPD should be diagnosed and studied in adolescents (Greenfield et al., 2015). To date, experimental data in adolescents with BPD are scarce. The pathophysiological mechanisms underlying the development of BPD and the physiological characteristics of the early stages of the diseases remain poorly understood. However, it has been proposed that stress may be a dimension of particular interest in BPD patients (Bourvis et al., 2017). First, exposure to stressors early in life has been repeatedly found to be associated with the onset of the disorder (Gunderson et al., 2018). Second, patients who develop BPD may also develop a peculiar physiological response to acute stress (Perez-Rodriguez et al., 2018). Hence, some authors hypothesize that BPD is a developmental disorder of the stress axis (Bourvis et al., 2017).

A narrow definition of stress describes this phenomenon as "a condition where an environmental demand exceeds the natural regulatory capacities of an organism, in particular in situations that include unpredictability and uncontrollability" (Koolhaas et al., 2011). Stress reactivity is indeed a complex phenomenon that is associated with multiple and multimodal expressions. The global responses to stressors include neurovegetative, neurohormonal, behavioral, cognitive and affective features. Despite the widespread research in this field, some aspects are consistent across researchers. The stress response system participates in species survival and individual adaptation. This implies immediate changes in both neurobiological and behavioral levels. The biological response relates to changes in the autonomic nervous system (ANS) (immediate response) and the hypothalamic-pituitary-adrenal (HPA) pathway that encode numerous short- and long-term cascades (Szabo et al., 2012). Stress appears to have three main biological functions: it coordinates the organism's allostatic physical and psychosocial responses to external and internal challenges; it encodes, filters and reduces information about the organism's environment; and it regulates the physiology and behavior of a large range of social interaction areas (e.g., parenting, risk-taking behavior in social context, coping behavior, reproduction, affiliation) in both the short term and long term (Del Giudice et al., 2011).

In all species, stress is an internal mechanism to adapt to danger, and it may induce individual behavioral reactions. In animals that engage in social interaction, reactions to stress are also associated with inter individual communication. For example, alarm calls for protection can be measured in pups during early separation using ultrasounds (Nagasawa et al., 2012). Also, they can be measured in Velvet monkeys, which use different types of vocalizations depending on the threat (Seyfarth et al. 1980). In humans, this "alarm call function" has been widely studied in infants (e.g., Soltis 2004; Weisman et al., 2016). Therefore, stress may be studied from both an internal perspective (self-perception) and an external/interactive perspective (heteroperception) (Spodenkiewicz et al., 2018). The dissociation between self- and heteroperception might be of particular interest for adolescents with BPD. Indeed, many authors have reported a frequent dissociation between the two sides of emotional state perception in individuals with BPD (Zanarini et al., 2007;

Dammann et al., 2011; Spodenkiewicz et al., 2013; Morey, 2014). This dissociation seems to derive from distortions in both the perception of environmental stimuli and the perception of one's internal state (Gunderson et al., 2018). Moreover, adolescence is a sensitive period during which insight drastically improves. Studying the ability to correctly assess one's internal state among adolescents with BPD therefore seems of particular interest. We hypothesize that altered stress reactivity and self-perception might reflect both the emotional instability and lack of insight of adolescents with BPD. One recent study using a multimodal assessment approach showed that ANS dysfunction monitored through heart rate variability (HRV) was associated with symptom severity in adolescents with BPD (Weise et al., 2020).

Fineberg et al. (2017) recently reviewed how computational psychiatry approach could be relevant to explore the interplay between BPD and social neurosciences. Here, we will specifically explore experimentally response to acute stress. Behavior and interaction imaging is a promising domain of affective computing that can be used to explore behavior (Vinciarelli et al., 2009) and psychiatric conditions (Leclère et al., 2016). Previous work using multimodal recordings of short-term stress responses in healthy young adults using automatized classification methods based on machine learning showed that (i) classification performances were very high, (ii) self-perception and heteroperception were similar but different phenomena (Aigrain, 2016), and (iii) self-perception classification was mainly based on physiological features, while heteroperception was mainly based on behavioral features (Spodenkiewicz et al., 2018).

Herein, we used a similar approach to investigate self- and heteroperception in adolescents with BPD when compared to healthy control (HC) adolescents. We hypothesized that (i) classification performances will remain satisfactory in this younger population; (ii) adolescents with BPD will display a higher reactivity to stressors than HCs; and (iii) adolescents with BPD will display an altered self-perception of stress reactivity. In addition, to explore the HPA response, we examined salivary cortisol. Based on previous research on BPD (Bourvis et al., 2017), we hypothesized that adolescents with BPD would have higher basal cortisol levels and an attenuated cortisol response.

METHODS

Participants and ethics

The design of the study was approved by the *Comité de Protection des Personnes* CPP Ouest 6 (ethical committee authorization number: 989 HPS2). We enrolled 40 adolescents aged 13-18 years old in the study from October 2017 to January 2019. All patients (N=20) were recruited from the Child and Adolescent Psychiatry Department at Pitié-Salpêtrière in Paris, France. They were matched for age and sex to 20 HC adolescents. All participants and their parents provided informed consent to participate. All patients (n=20) were diagnosed with BPD by a senior psychiatrist. Diagnoses were based on a direct clinical assessment based on the DSM-5 criteria combined with a standardized clinical questionnaire (Ab-DIB) (Guilé et al., 2009). To ensure that patients had BPD, we included patients who had an Ab-DIB score of 10 or higher. Healthy controls (n=20) were recruited from the general population and were not diagnosed with BPD (Ab-DIB score < 7) or any psychiatric disorder. To describe the clinical characteristics of the patients, we used the following measures: the Mini Neuropsychiatric Interview (MINI) for adolescents was used to assess potential disorders associated with BPD (Sheehan et al., 2010), the Global Assessment of Functioning (GAF) was used to assess overall severity (Schorre and Vandvik, 2004), the State-Trait Anxiety Inventory (STAI-form YB) was used to assess trait anxiety (Spielberger et al., 1983), the Relationship Scales Questionnaire (RSQ) was used to assess attachment (Guédeney et al., 2010), the PHQ-9 (Spitzer et al., 1999) was used to assess depressive symptoms and the Childhood Trauma Questionnaire was used to assess lifetime traumatic experiences (Paquette et al., 2004). The RSQ consists of 17 items to assess attachment patterns as continuous scores. Four scores are calculated for secure attachment, fearful attachment, preoccupied attachment, and dismissive attachment. The PHQ-9 is the depression module of the self-administered version of the PRIME-MD diagnostic instrument for common mental disorders. It scores each of the 9 DSM-IV criteria as "0" (not at all) to "3" (nearly every day). The CTQ is a self-report measure that assesses experiences of physical, emotional, and sexual abuse and physical and emotional neglect, as well as related aspects of the child-rearing environment. The participants' main characteristics are summarized in table 1. As expected, patients

with BPD did not differ significantly from HC for age and gender given the matching procedure. However, they showed significant differences in almost all other sociodemographic, clinical and dimensional characteristics (see details in table 1).

Stress task and data acquisition

One of the best ways to induce stress is to have a subject experiencing a cognitive load, such as a mathematical test, while being socially evaluated (Dickerson and Kemeny, 2004). All participants performed a socially evaluated mental arithmetic test. The task was inspired by a previously described mental arithmetic task used for the validation of the Mathematical Anxiety Rating Scale (Ashcraft and Faust, 1994). The task was composed of six steps with increasing difficulty, with a break period of 5 seconds between each step. The total duration of the task was 12 minutes. The task was similar to that of Spodenkiewicz et al. (Spodenkiewicz et al., 2018) except the calculations used herein were simplified and adapted for younger individuals. The experimental task and setup are fully described in a short video sequence available online (http://doi.org/10.5281/zenodo.3817212).

During the task, each participant was video recorded using both a Kinect® device and an HD video. Each participant was also wearing a portable device (Nexus10, Mind Media lab) to record physiological data. Several features were extracted online through specific sensors and algorithms based on previous research (Aigrain, 2016). These data are listed in Table 2. From the Kinect recording, we extracted 15 features and metrics (means) associated with body movements of the participants using homemade software (see below). From the HD video recording of the face, we extracted 12 facial landmarks/action units (AU) and 24 metrics (means, SD) associated with facial movements using homemade software (see below). From the Nexus10 recording, we extracted 13 features and 52 metrics (mean, SD, minimum, maximum) associated with physiological parameters (blood pressure, heart rate, respiratory frequency, skin conductance, body temperature) using the BioTrace+ software (MIndMedia Lab).

To assess stress during the task and distinguish self- vs. heteroperceived stress, we followed the method developed in Spodenkiewicz et al. (2018). However, for heteroperception, it was not ethically possible to use crowd sourcing given the

vulnerability of adolescents with BPD. The level of stress of each participant was evaluated at each step by a psychiatrist who was present in the experimental room using a Likert scale ranging from 0 to 5 (0 = no stress at all; 5 = highest possible level of stress). To validate the heteroperception assessment, we asked another clinician to blindly rate 30 videos, and we measured the interrater reliability. The interrater reliability was excellent: Cohen's Kappa measuring dichotomic agreement (stress vs. nonstress) was equal to 0.813, and the correlation when using a continuous score was equal to 0.88 ($p < 0.00001$). For self-perceived stress, the level of stress was assessed by the participants themselves as in Spodenkiewicz et al. (2018). Just after the experimental task, each participant watched his/her own video and was asked to rate their level of stress at each step on a scale ranging from 1 to 5.

Hormonal markers of stress

Saliva samples were collected using "Salivette® for Cortisol". According to protocol, eating, drinking tea or coffee, and brushing teeth were prohibited for 3h prior to sampling. Saliva was collected just before the test, 5 min and 30 min after the end of the task. Salivette® were centrifuged 10 min at 3,000 g, then aliquoted and stored at -80°C until their measurement of cortisol. The UPLC/MS/MS consisted of a Xevo TQD from Waters including a column Acquity UPLC® BEH C18 1.7 μm. The hardware was controlled by MassLynx software. Cortisol and deuterated cortisol-D4 were purchased from ChromSystems. Six calibration standards were used covering the range 0.5-60 ug/L. Aliquots of 120 μl (Calibration standards, blank controls, quality controls and saliva samples) were treated with 120 μl of extraction solution from ChromSystems thoroughly mixed during 10 min at 2000 RPM. Then 200 μl were centrifuged 15 min at 1500 g. The supernatants were transferred to autosamplers vials. The sample (20 μl) was loaded onto the column. The mobile phase comprised a binary solvent system: 100% H_2O containing 0.14 g/l of acetate ammonium and 1 ml formic acid (Solvent A) and 100% MeOH containing 0.14 g/l of acetate ammonium and 1 ml Formic acid (Solvent B). The initial solvent composition was 80% A and 20% B. The mobile phase gradient profile involved three steps: increasing from the initial conditions to 100 B within 2 min 50 sec and then maintaining 100% B within 1 min 20 sec then return to 80% A in 10 sec. The total run time was 10 min injection to

injection. The flow rate was 0.5 mL/min. The electrospray ionization (ESI) source was operated in the positive-ion mode at a capillary voltage of 3 kV and cone voltage of 35 V. The ion source and the desolvation temperatures were maintained at 400°C. Cortisol were detected and quantified in the positive-ion mode; product ion response was measured in multireaction monitoring (MRM) mode at set transitions mass to charge (m/z) of 363.1 → 120.8.

Data analysis via homemade algorithms

Due to ethical requirements not to store videos of patients, we did not use offline analysis as in Aigrain et al. (2016) but instead extracted online all relevant features listed in table 2. The system was completely written using Python 2.7. Python is an interpreted general-purpose programming language with a broad number of additional packages (libraries) that extend its basic features. Python interpreters are available for several operating systems as well as for mobile devices. Python was also chosen for its availability for machine learning and image processing capabilities and for its computer vision external libraries. The following Python libraries were used in the development phase: sys, os, glob, Dlib (King, 2009), NumPy (Walt, 2011), Scikit-image (Van, 2014), and Scikit-learn (Pedregosa, 2011). The Dlib library is a recently developed toolkit that provides machine-learning algorithms and computer vision tools to create cutting-edge software solutions. It is used in academia and industry in an extensive variety of applications, such as mobile devices, classification, computer vision for robotics, and embedded devices. Scikit-image is a library of image processing algorithms that consists of algorithms for geometric transformations, color space modification, filtering, normalization, and segmentation. The Scikit-learn library extends Python with machine learning-dedicated algorithms such as classification, regression, and clustering. The Python interpreter and its external libraries were installed on the same machine where the system has been developed on an Oracle VirtualBox virtual machine (VM). The VM had the following characteristics: 2 CPU cores each at 1.8 GHz, 2048 MB of RAM, a 20 GB virtual solid-state disk, and a GNU/Linux LUbuntu 16.04 LTS 64 bit.

From a software point of view, the proposed system includes several modules that use specific computer vision and machine learning algorithms: (1) the

acquisition and preprocessing module; (2) the feature extraction module for all features listed in Table 2 and validated in Aigrain et al. (2016); and (3) the classification module. Steps 1 and 2 do not require any human intervention. Sept 3 requires the intervention of a human rater for borderline symptomatology, self- and heteroperception of stress (see details below). Given raw files from devices, the system was able to preprocess the raw data to adapt them for the next software modules. The extracted feature vectors of the data were used as input to the classification module. The proposed system pipeline is depicted in Figure 1.

Classification of BPD and healthy adolescents

In this work, a new set of features has been proposed that brings uncertainty regarding the best way to perform the classification step. Therefore, the first step of our machine learning classification was to determine the most appropriate algorithm given the nature of the extracted features. Indeed, algorithms show variable performance depending on the peculiarities of the input data. Four machine learning algorithms were compared to select the best one suited for the extracted features: i) support vector machines (SVMs) (Boser et al. 1992) that have been used as baseline because previously used in Aigrain et al. (2016); ii) naive Bayes (Webb, 2011); iii) AdaBoost (Schapire, 2013); iv) and C4.5 (Quinlan, 2014).

SVM estimates optimal separating hyperplanes in a high-dimensional space between adolescents with BPD and healthy individuals. The hyperplane that maximizes the distance between the training data of the two classes is the best one. If the training data can be separated in a finite-dimensional space, then the data are linearly separable, and a linear kernel is used. In the classification problem, naive Bayes classifiers are based on the Bayes rule together with a strong assumption of independence between the features. AdaBoost performs binary classification using a machine-learning meta-algorithm. This algorithm uses other weak algorithm results that combine in a weighted sum to obtain a boosted classification output. The C4.5 algorithm builds a decision tree from training data using information gain (entropy reduction) for tree splitting. For each node, the algorithm selects the most effective features to split the training set into two classes. In the decision tree, each node is a

test on a feature of the training set, each branch represents the output of a test, and each terminal node or leaf is the class to predict.

To assess the binary classification (BPD vs. HC), we used the accuracy as a metric since we had two perfectly balanced samples with 20 individuals each. Adolescents with BPD are what the system is trained to classify and what the system aims to identify. Cases of BPD that are correctly classified as BPD are true positives (TPs), whereas cases of BPD that are classified as HCs are called false negatives (FNs). Conversely, HCs classified as cases of BPD are false positives (FPs), and HCs classified correctly as HCs are true negative (TNs). The accuracy formula is:

$$accuracy = \frac{TP + TN}{TP + TN + FP + FN}$$

Table 3 shows how different machine learning algorithms predicted cases of BPD vs HCs. The table indicates that support vector machines, naive Bayes, and decision trees yield efficient results, but AdaBoost had the best accuracy and outperformed other algorithms.

Classification of stress in BPD and healthy adolescents

The experimental task was based on both individual characteristics (BPD vs. healthy) and responses to stress. The first binary classification only intended to select the algorithm that best fit our data. To assess stress, AdaBoost was the only machine learning algorithm used in the following analyses. However, as responses to stress were highly heterogeneous within individuals and within perspective (self- vs. heteroperception), we expected an unbalanced dataset to run classifications. In this case, the accuracy was not valid as a metric, and the weighted arithmetic mean of the F-score for both classes was chosen as the performance metric. The weighted arithmetic mean of the F-score allows considering the recall and precision of both classes. In this case, the metric based on the mean also takes into account true negative values and not only positive classes. Once the metric to evaluate the classifiers was defined, Student's t-test was conducted on the metric. Mathematically, the F1-score is the harmonic mean of precision and recall, and the F-score ranges from 0 (worst) to 1 (best). The formula to calculate the F-score is:

$F1 = 2 \times \frac{PPV \times TPR}{PPV + TPR}$ where PPV is the positive predictive value and TPR is the true positive rate.

The machine learning procedure was applied several times for the prediction of self- and heteroperceived stress among BPD patients and HCs. For the first two procedures, we only used unimodal features: body movement features, physiological features. For the second procedure, we used all movements features meaning body movement features + facial landmarks. For the fourth and last procedure, we used multimodal features meaning body movement features + face landmarks + physiological features.

RESULTS

Human rating of stress during the experiment

For each participant, all steps of the experiment were assessed both by the external observer during the experiment (heteroperception of stress) and after the task by the participant itself (self-perception of stress). The results are summarized in Figure 2. From both points of view, adolescents with BPD had a more stressful experience than the HCs (p<0.001). A total of 77.5% of the sequences were rated as stressful in the BPD group (vs. 39.16% for the HC) by external raters (heteroperception). Similarly, 63.5% of the sequences were acknowledged as stressful by BPD participants (self-perception) vs. only 20.83% by HCs (p<0.001). In addition, in both groups, the self-perception of stress was lower than the heteroperception of stress (BPD: p=0.02; HC: p=0.002).

Salivary cortisol

Salivary cortisol changes during the experiment are summarized in Figure S1 and Table S1 (supplementary material). To explore changes during the experiment in each group, we used a mixed model (formula: cortisol ~ group + time + group*time + (1|id_sujet)). At baseline, adolescents with BPD tended to have a higher salivary cortisol concentration (2.58 (±2.06) vs. 1.85 (±1.42) ng/ml, p=0.10). However, the cortisol response was absent on average and did not differ between groups (Table S2 supplementary material). An exploration of cortisol levels over time in adolescents

with BPD even showed a significant decrease in salivary cortisol after the arithmetic test (Table S1).

Machine learning performance according to perception and clinical status

We compared the performance and reliability of the classifier using the F1 metric for heteroperception and self-perception in both groups (BPD vs. HC). This performance was calculated for when the classifier was based on body movement features only, both body movement and facial landmark features, physiological features only and all types of features combined together (Figure 3). In all cases, the use of a multimodal approach had an excellent predictive value (F1 scores above 0.85), suggesting that our approach was acceptable. It is likely that the moderate prediction (F1 scores approximately 0.7) in the selection of the best classifier to separate cases of BPD and HCs was related to the fact that we did not take into account the distinction between stress and nonstress video sequences (see method section).

There were two striking observations in addition to the high classification scores reached using the different combinations of features. First, in both groups (BPD and HC), we found that behavioral features reached higher classification scores for heteroperception than for self-perception of stress. In contrast, classification scores based on physiological features yielded better scores for self-perception than for heteroperception of stress. Second, we found the opposite effect regarding the self-perception and heteroperception of stress between the two groups. Across all classifications, we found better F1 scores for heteroperception than self-perception of stress in individuals with BPD. In contrast, we found the opposite in HCs: across all classifications, F1 scores for self-perception were better than those for heteroperception of stress.

F1 scores for each feature are listed in Table S3 (supplementary material). Interestingly, most features had F1 scores ranging from 0.4 to 0.7, meaning that it is the combination of features that permitted classifications to reach F1 scores of 0.85 and above. However, only a few features had F1 scores above 0.7. They all belonged to the classification of adolescents with BPD in heteroperception. Two features were related to the quantity of movement of the head, two other features were related

with periods of high activity, one feature was related with posture change, one feature was related with the quantity of movement for both hands, and the last feature was related with the quantity of movement computed with the skeleton. This means that stress was easily detectable through motor behavior in adolescents with BPD.

DISCUSSION

Summary of the results

The results show that our task is an efficient paradigm to assess reactions to acute stress in both HCs and adolescents with BPD. Given the lack of cortisol response in both groups, the task mainly triggered the autonomic nervous system response (or immediate response) rather than the HPA response (short- and long-term cascades) (Szabo et al., 2012). More importantly, it appears that our affective computing approach for stress (Aigrain et al., 2016; Vinciarelli et al., 2009) yielded similar machine learning classifications as in adults: multimodal classification based on both physiological data plus movement features yielded excellent F1 scores; classification based on physiological features alone yielded better F1 scores for self-perception; and classification based on behavioral features alone yielded better F1 scores for heteroperception (Spodenkiewicz et al., 2018). Adolescents with BPD displayed higher stress levels at baseline, as evidenced by an increased salivary cortisol, but these levels were not significantly different than the levels among HC. Adolescents with BPD also experienced more stress during the mental arithmetic test (Figure 2). Finally, as hypothesized, human ratings and affective computing models yielded opposite results regarding self- and heteroperceived stress in adolescents with BPD compared to HCs. Adolescents with BPD had higher levels of heteroperceived stress than self-perceived stress. Similarly, affective computing led to better classification of heteroperceived stress in adolescents with BPD.

Stress and BPD

As stated above, we observed a significant difference in stress levels between the two groups. At baseline, the common biological marker salivary cortisol tended

to be higher among adolescents with BPD. More importantly, during the experiment, adolescents with BPD had a stronger reaction to the stressor than HCs according to both self-perceptions and heteroperceptions. For most clinicians, this is well known: BPD patients, especially young BPD patients, are prone to high levels of stress, and stress episodes may lead to specific impulsive and harmful behaviors (e.g., self-harm, suicidal attempts) in this population (Leichsenring et al., 2011). Patients' personal histories are often marked by stressful or traumatic experiences (Zanarini et al., 2000). This was also the case in our sample (see Table 1). Moreover, clinical signs of the disorder include both chronic and acute features. Acute features (e.g., transient cognitive distortion, anger, impulsivity, and self-harm behavior) are mostly triggered by acute stressful situations (Bourvis et al., 2017). In our sample, such features included suicide, as indicated by the high rate of suicidality. Chronic features include insecure attachment, self-image and interpersonal relationships. Higher PHQ scores among the adolescents with BPD in our sample indicate that many had fearful attachment style (Levy et al., 2005).

In addition to clinical aspects, responses to stress can also be discussed in terms of response levels. Given our experiment, we will discuss the hormonal, behavioral and subjective responses. First, we did not find higher baseline cortisol levels in the BPD adolescent group as the statistical comparison only reach a tendency. This is not consistent with previous findings in adults in which baseline cortisol levels are higher in BDP individuals (Lieb et al., 2004, Wingenfeld et al., 2007). To our knowledge, our experiment is the first evidence of salivary cortisol in adolescents with BPD, thus suggesting that this feature may be observed in the early stages of the disorder. However, a larger sample is needed to confirm this tendency given the wide ranges found in both groups of adolescents (see Figure S1). In adults, several comorbid disorders, such as depression and posttraumatic stress disorder, have been shown to influence cortisol levels in individuals with BPD (Zimmerman and Choi-Kain, 2009). Depression is associated with higher basal cortisol levels, whereas posttraumatic stress disorder is associated with lower basal cortisol rates (Wingenfeld et al., 2007b). Our sample was indeed characterized by a high rate of depression and suicidality (Table 1). As Meyer et al. (2016) suggested in an adult study, interaction between traumatic experiences, autonomic nervous system

response to stress, and psychopathology is complex. Alterations in heart rate variability might be related to early life maltreatment or associated psychological factors rather than diagnostic entities. We could not explore the same dimensions (e.g., RSQ or CTQ scores) in our sample due to power limitation (see below).

Second, the behavioral response to stress in BPD has been associated with a lack of locus of control and impulsivity (Bourvis et al., 2017). Impulsivity is a core feature of BPD, and in contrast to other psychiatric conditions that are also characterized by some impulsivity (such as attention deficit hyperactivity disorder (ADHD)), impulse control deficits in BPD occur specifically under stressful conditions (Krause-Utz et al., 2016). In our experiment, this behavioral response is also the one mostly approached by an external observer. Indeed, we obtained higher performances of the stress classifier by using behavioral cues only in BPD patients vs. HCs (Figure 3). This is in line with Krause-Utz (2016), who showed that BPD patients performed worse at action with holding tasks than other groups (HCs or ADHD patients) in stressful situations. Interestingly, the most contributing features for the performance classification are those linked with lack of action regarding holding or motor control/stability (Quantity of Movement for the Head, Number of periods and Mean Duration of High Activity, Number of posture changes) (Supplement material S3).

Finally, in terms of phenomenological perception of stressful stimuli and the related subjective experience, the literature is very limited. Most experimental works examining BPD focus on the subjective experience of pain (Bourvis et al. 2017). We are aware that it remains a matter of debate whether pain can be considered an extreme version of stress and can be studied as such or whether the specific involvement of the pain matrix system makes such parallels irrelevant. However, we believe that pain may be relevant to the increased use of nonsuicidal self-injury and cutting in BPD patients, as it appears that nociceptive input specifically leads to stress reduction (Naoum et al., 2016). The same group used an experimental procedure and showed that among BPD patients, the nociceptive input led to stress reduction and that painful stimuli led to a greater stress reduction in BPD patients compared with HCs (Willis et al. 2017). Several studies using evoked potentials have shown that the threshold for a stimulation to be considered

"painful" was higher in BPD patients (Schmahl and Baumgärtner, 2015; Ludäscheret al. 2015). However, the perception of the intensity of the stimulation was unchanged. Thus, the perception in itself does not seem to be altered but rather the subjective experience of pain, namely, what triggers the shift from an uncomfortable sensation to a painful experience. To further discuss self-perception of stress in BPD, we propose discussing it using the concept of a lack of insight, a key feature in the context of the patient-therapist relationship among BPD patients (Høglend, 2014).

Lack of insights and BPD

One of the core features of BPD patients is an impaired ability to recognize and think about their own bodily and mental states as well as those of others. Both Linehan's biopsychosocial theory and Fonagy and Luyten's failed mentalization theory have emphasized the difficulty that BPD patients have with identifying, labeling, and describing emotions and the phenomenological experience of one's self (Gunderson et al., 2018). These impairments have been confirmed by psychometric studies (see (Löffler et al., 2018 for a review). For example, BPD patients have been shown to have a high level of alexithymia (inability to label emotions) (Lysaker et al., 2017; Modestin et al., 2004; New et al., 2012).

The phenomenology of lack of insights is at least two-fold. In some cases, it could be an avoidant cognitive strategy as "ignoring the problem". Knafo et al. (2015) showed that in the immediate aftermath of a suicidal crisis, BPD adolescents while experiencing high levels of suicidal ideation and impulse phobia, did use predominantly avoidant cognitive coping strategies. In addition, recent developments have stressed the importance of interoceptive deficits in BPD. Interoception refers to the processing and awareness of afferent information from the body. This process has been related to alexithymia (see (Löffler et al., 2018) for a review). As said previously, among BPD patients, pain hyposensitivity has been demonstrated as a prominent interoceptive deficit (Chung et al., 2020). To date, a few studies have investigated the interoceptive capability of BPD patients beyond pain perception. With respect to heartbeats, the results are contradictory: one study found no change in the interoceptive awareness of heartbeats in BPD patients (Hart et al., 2013), whereas a second study revealed a diminished amplitude of heartbeat-

evoked potentials at the neurophysiological level in BPD patients, indicating an alteration of interoceptive processing (Müller et al., 2015). Recently, Neustadter et al. (2019) employed the rubber hand illusion to manipulate sense of body ownership in BPD adults. They found that patients with BPD maintained illusion susceptibility in the asynchronous condition and were more susceptible to illusory body ownership than HC. Given the impairment of the physiological stress axis related to childhood adversity and the aforementioned alterations related to integration of bodily signals in BPD, some researchers have suggested a broader impairment of the brain-body axis in this disorder (Löffler et al., 2018; Bourvis et al., 2017; Neustadter et al., 2019). Our study was an attempt to investigate the contribution of a broad range of bodily signals, including neurovegetative, hormonal and behavioral signals, to the awareness of one's own emotional state of stress in adolescents with BPD.

The models of affective computing were better at predicting the level of stress perceived by an external observer in adolescents with BPD (heteroperception). The opposite finding was observed for HC adolescents as well as for adults (Spodenkievcz et al. 2018). This means that external observers' ratings are more accurate than those of BPD patients themselves. The opposite trend is observed in HCs. These findings are consistent with clinical observations in BPD patients (Guilé et al., 2018). In stressful contexts, their behavior may be characterized by hyperarousal, disruption, and frequent outbursts of rage that are obvious to any external observer. Consequently, it may be easier for an external observer to label the level of stress among BPD patients than among HCs. As said previously, the hyperarousal of motor responses in BPD patients is likely to be related to the behavioral features that are best detected by affective computing (see the list of behaviors related to quantity of movements, Table S3).

However, adolescents with BPD may also be less able to rate their level of stress accurately due to a lack of recognition of their bodily signals (Gunderson et al., 2018; Löffler et al., 2018). In line with this second possibility, our results regarding self-perception suggest that BPD patients' ratings are systematically less accurate than those of HCs. Our results extend the qualitative literature suggesting that adolescent BPD patients have a deficit of self-perception for a broad range of stress-related bodily signals (Bourvis et al., 2016). This blunted sensitivity to bodily stress

signals combined with emotional awareness deficit might contribute to the development of incoherent self-other representations in BPD (Löffler et al., 2018). Given that BPD is conceptualized as a disorder of self and interpersonal functioning (Bender & Skodol, 2007; Høglend, 2014), emotional and bodily awareness and regulation are a critical focus in therapy to improve interpersonal functioning (see (Euler et al., 2019) for a review).

Finally, one of the most striking interpersonal phenomena in BPD is the defensive mechanisms of splitting and related projective identifications. These concepts have rarely been addressed in the experimental literature. Nevertheless, they are the focus of extensive psychodynamic literature (Kernberg, 1975; Corcos et al., 2013). These defensive mechanisms could be seen as desperate attempts to regain control in the context of relationships that are still under threat of real or imagined abandonment. In line with this hypothesis, studies in the general population have shown a global loss of sense of control in the context of environmental adversities and/or stress dysregulation (Pepper and Nettle, 2017), the latter being the hallmark of BPD. Future studies should investigate how this loss of control relates to interpersonal dysfunction in BPD.

Limitations

The study should be interpreted in light of its limitations. First, despite being driven by several clinical hypotheses, we are aware that machine learning classification may appear difficult to interpret. We cannot exclude the possibility that the chosen algorithm AdaBoost overfits the behavioral data that are associated with heteroperception. Overfitting is a common limitation in machine learning that has been discussed with respect to psychiatry (Bennett et al., 2019). However, we are reassured by the clinical relevance of the results, the opposite pattern that was found in HC adolescents, and the fact that this opposite pattern was similar to previous research in young healthy adults using another classifier (SVM) (Aigrain et al. 2016; Spodenkiewicz et al. 2018). Second, we are aware that the sample size is small. It was determined based on our first study and powered for the purpose of the experiment. However, it was not powered to explore whether other clinical dimensions (e.g., depression, suicidality, anxiety and attachment) or past history

(e.g., childhood trauma) were correlated with stress responses. Given previous studies in adults this should be further explored (Meyer et al., 2016). This is also a limit for generalization. Third, we compared BPD to HC controls and not to other subjects with another diagnosis (e.g. PTSD). So we cannot clarify whether our findings is specific or whether it is shared trans diagnostically. Given previous literature, we believe it is more likely the second hypothesis. Finally, in this experiment, self-perception refers to a higher-order metacognitive representation given that the participants had to rate their level of stress retrospectively by watching the video of their experiment after it was finished.

Conclusion

Adolescents with BPD are more sensitive to stress and show a lack of self-perception (or insight). In terms of clinical implications, our affective computing measures may help decipher hetero vs. self-perceptions of stress in natural settings and may offer external feedback during therapeutic interactions.

Declaration of interests
All authors except Dr Cohen declare no conflicts of interest.
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Author contributions
Study conception and design: MC, MS, DC; coordination and monitoring, data collection: NB, AA, GP, AB; statistical analysis, machine learning and interpretation of the data: GP, JA, DC, MC, NB,AA; biochemistry: NB, AA, JJB; drafting the manuscript: NB, AB, GP, JJB, DC. All authors read and approved the final manuscript.

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Table 1. Participants' sociodemographic and clinical characteristics			
	Borderline personality disorder (N=20)	**Healthy controls (N=20)**	**p (test)**
SOCIODEMOGRAPHIC CHARACTERISTICS			
Age, median [IQR]	15.79 [15.41; 16.30]	16.21 [15.78; 16.55]	0.1567 (t-test)
Gender (F/M), n (%)	12 (60)/8 (40)	12 (60)/8 (40)	NA
Living situation w/ both parents, n(%) (yes/no)	8 (40)/12 (60)	15 (79)/4 (21)	0.0135 (chi-squared test)
Education Grade repetition n(%) (yes/no)	9 (45)/11 (55)	0 (0)/20 (100)	0.00123 (Fisher's exact test)
CLINICAL CHARACTERISTICS			
Ab-DIB, mean (SD)	23.4 (10.3)	3.75 (4.4)	NA
Current comorbidities	Depression (N=7) Dysthymia (N=3) Anxiety disorder (N=10) Substance use (N=4)	Cannabis misuse (N=1)	NA
Past history	Depression (N=10) Dysthymia (N=2) Anxiety disorder (N=2) Substance use (N=4)	Depression (N=3) Anxiety disorder (N=2)	NA

Suicidality
    Suicide attempts, n(%) (yes/no)
    Non Suicidal Self-Injury, n(%) (yes/no)
	17 (85)/3 (15)
	
	14 (70)/6 (30)
		0 (0) /20 (100)
		
		0 (0) /20 (100)
			< 0.001 (Fisher's exact test)

DIMENSIONAL CHARACTERISTICS			
CTQ (childhood trauma), median [IQR]	49 [37; 61]	31 [27; 34]	< 0.001 (Wilcoxon rank sum test)
PHQ-9 (depressive symptoms), median [IQR]	10.5 [5.75; 15.25]	5 [2; 6]	0.0188 (Wilcoxon rank sum test)
STAI-YB (trait anxiety), median [IQR]	3 [2; 4]	2 [1; 2.5]	0.0118 (Wilcoxon rank sum test)
RSQ secure median [IQR]	14 [12; 15]	13 [9; 14]	0.1054 (Wilcoxon rank sum test)
RSQ fearful median [IQR]	10 [9; 11]	11 [9; 14]	0.0140 (Wilcoxon rank sum test)
RSQ preoccupied median [IQR]	11 [7; 15]	12 [10; 15]	0.7432 (Wilcoxon rank sum test)
RSQ dismissive median [IQR]	17 [13; 21]	15 [13; 20]	0.5058 (Wilcoxon rank sum test)

CTQ=Childhood Trauma Questionnaire; RSQ: Relationship Scales Questionnaire; Ado-DIB= Diagnostic Interview For Borderlines-adolescent; M=Male; F=Female
IQR= Interquartile range

Table 2. Extracted features for the classification of stress

Acronym	Definition	Metrics
	BODY MOVEMENT FEATURES	
HeM	Quantity of movement for the head	Mean
HeMZ	Quantity of movement for the head only along Z-axis	Mean
IQoM	Quantity of movement computed with the RGB frames	Mean
HAPC	Number of periods of high activity	Mean
HAPMD	Mean duration of periods of high activity	Mean
HAPMV	Mean highest value of periods of high activity	Mean
PCC	Number of posture changes	Mean
SQoM	Quantity of movement computed with the skeleton	Mean
HM	Quantity of movement for both hands	Mean
LHM	Quantity of movement for the left hand	Mean
RHM	Quantity of movement for the right hand	Mean
FTC	Number of times face touching with one hand occurred	Mean
FT2HC	Number of times face touching with two hands occurred	Mean
FTMD	Mean duration of face touching with one hand	Mean
FT2HMD	Mean duration of face touching with two hands	Mean
	FACIAL LANDMARK/ACTION UNIT FEATURES	
AU1	Inner Brow Raiser	Mean, SD
AU2	Outer Brow Raiser	Mean, SD
AU4	Brow Lowerer	Mean, SD
AU5	Upper Lid Raiser	Mean, SD
AU6	Cheek Raiser	Mean, SD
AU9	Nose Wrinkler	Mean, SD
AU12	Lip Corner Puller	Mean, SD
AU15	Lip Corner Depressor	Mean, SD
AU17	Chin Raiser	Mean, SD
AU20	Lip Stretcher	Mean, SD
AU25	Lips Part	Mean, SD
AU26	Jaw Drop	Mean, SD
	PHYSIOLOGICAL FEATURES	
BVP	Blood Volume Pulse	Mean, SD, Min, Max
BVPA	Blood Volume Pulse Amplitude	Mean, SD, Min, Max
GSR	Galvanic Skin Response	Mean, SD, Min, Max
HR	Heart Rate Variability	Mean, SD, Min, Max
HRVA	Heart Rate Variability Amplitude	Mean, SD, Min, Max
HRV-LF%	Heart Rate Variability Low Frequency zone	Mean, SD, Min, Max
HRV-RMSSD	Heart Rate Variability square root of the mean squared difference between adjacent N-N intervals	Mean, SD, Min, Max
HRV-SDNN	Heart Rate Variability Standard Deviation of Normal to Normal intervals	Mean, SD, Min, Max
RSP	Chest and abdominal Respiration	Mean, SD, Min, Max
RSPA	Chest and abdominal Respiration Amplitude	Mean, SD, Min, Max
RSPR	Chest and abdominal Respiration Rate	Mean, SD, Min, Max
RSP+HR	Level of coherence between the Respiration and the Heart Rate	Mean, SD, Min, Max
TMP	Temperature	Mean, SD, Min, Max

Tableau 3. Accuracy of machine learning methods in predicting the videos (n=240), cases of BPD (N=20) vs. healthy controls (N=20) using behavioral features during the stress experiment

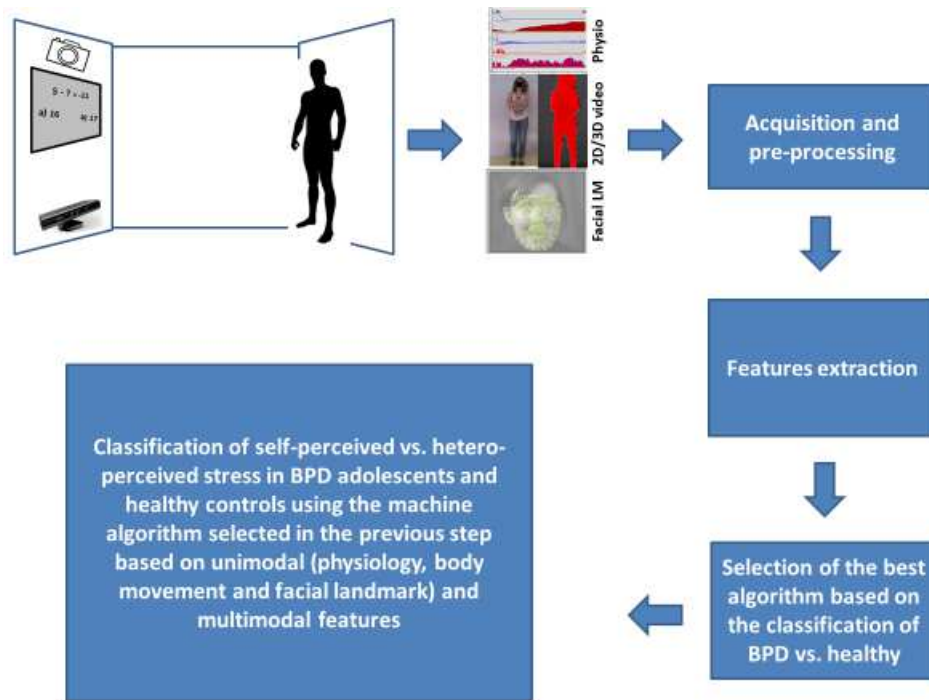|	SVM	Naive Bayes	AdaBoost	C4.5
Accuracy	61.8%	65.97%	73.61%	65.27%
t-test	Reference	-1.54	-5.73	-4.28
p-value	Reference	0.125	0.00001	0.000028

Fig. 1. Pipeline of the proposed system. The steps of the pipeline are acquisition and preprocessing, feature extraction, and classification.
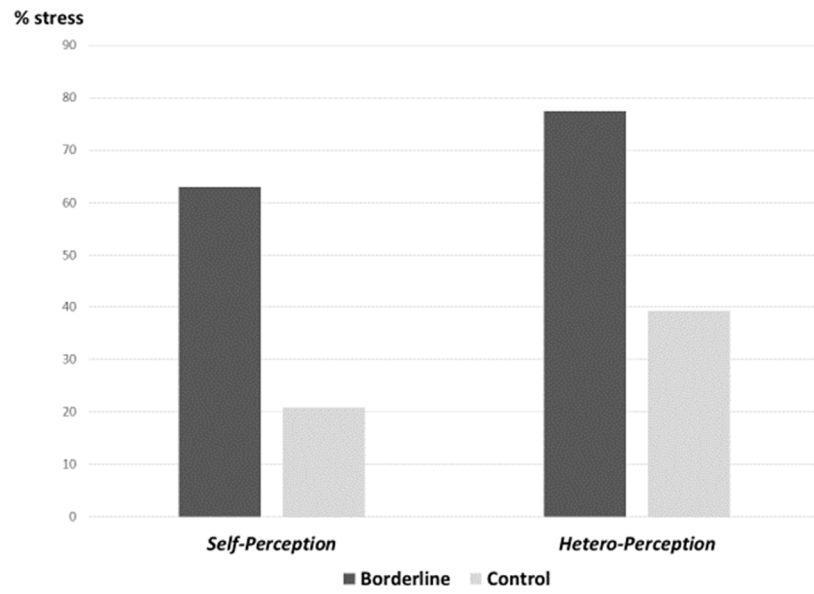
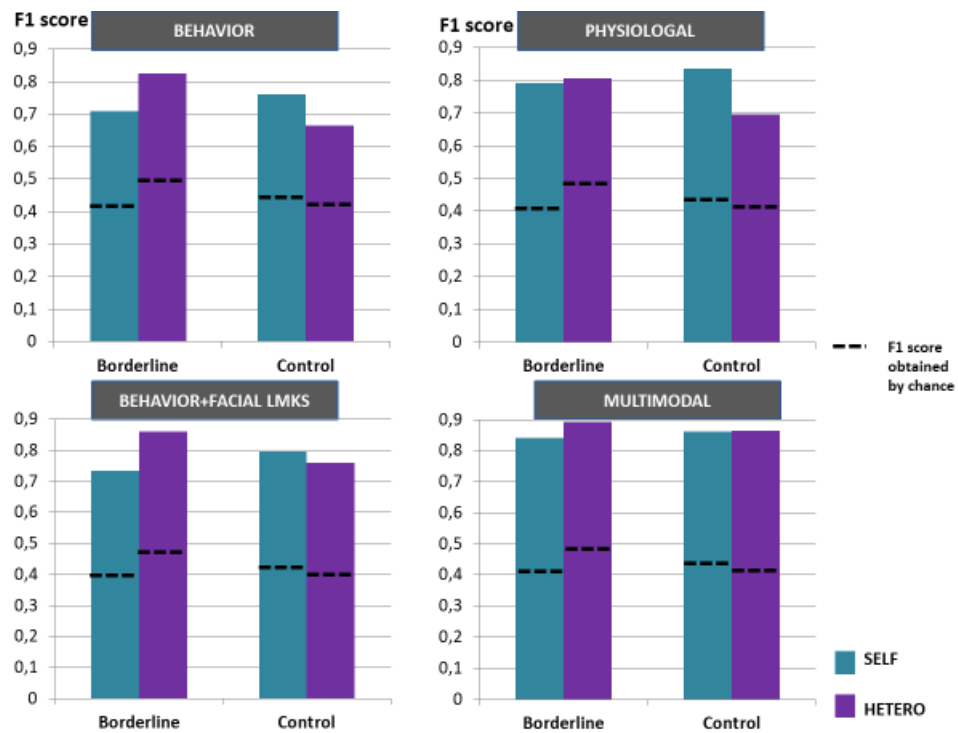**Figure 2. Human rating of stress during the experiment**

Figure 3. Prediction of stress (F1 score) using machine learning based on unimodal and multimodal features according to perception (hetero- vs. self-perception) and clinical status (BPD vs. HC)

Physio

2D/3D video

Facial LM

Acquisition and pre-processing

Features extraction

Selection of the best algorithm based on the classification of BPD vs. healthy

Classification of self-perceived vs. hetero-perceived stress in BPD adolescents and healthy controls using the machine algorithm selected in the previous step based on unimodal (physiology, body movement and facial landmark) and multimodal features

5 - ? = -11

a) 16   b) 17

F1 score — BEHAVIOR

Borderline | Control

F1 score — PHYSIOLOGAL

Borderline | Control

BEHAVIOR+FACIAL LMKS

Borderline | Control

MULTIMODAL

Borderline | Control

- - - **F1 score obtained by chance**

■ **SELF**

■ **HETERO**