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Exploring psychophysiological indices of disruptive behavior disorders and their subtypes of aggression

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ABSTRACT

Background: Psychophysiological measures of arousal are often considered as potential biomarkers for disruptive behavior disorder (DBD). Nevertheless, the evidence is mixed, possibly reflecting the heterogeneity of DBD and different subtypes of aggression. Additionally, arousal measures of the central nervous system (e.g. electroencephalogram: EEG) are underrepresented compared to peripheral ones (heart rate: HR; skin conductance: SC).
Methods: We recorded HR, SC, and EEG (frequency band power at three electrodes Fz, Cz, Pz) in 49 participants with DBD, and 15 typically developing peers during two resting state and an emotional task condition. Group differences were assessed by a repeated measure ANOVA and regression analyses were applied to evaluate subtype-specific patterns.
Results: Our results showed higher mean HR activity in DBD participants, which was however driven by medicated participants and no significant group differences were found for SC. Interestingly, a significant group x frequency band interaction emerged for the EEG. DBD youth showed lower alpha activity. Regression analyses showed that higher theta and lower alpha band activity were related to more general aggression scores and higher delta and lower beta activity predicted proactive aggression.
Conclusions: The lack of robust and significant differences for peripheral measurements (HR and SC) fits with previous mixed findings for externalizing disorders. Our results suggest that EEG measurements might be more sensitive to detect group differences and higher delta and lower beta activity might represent an index of a proactive subtype of aggression.

1. Introduction

Disruptive behavior disorders (DBD), which include oppositional defiant disorder (ODD) and conduct disorder (CD), are among the most commonly diagnosed mental health conditions in youth (Loeber et al., 2000) with a prevalence rate ranging from 2% to 4% (Polanczyk et al., 2015). However, these disorders are some of the less systematically studied psychiatric conditions (Fairchild et al., 2019), despite that DBDs are among the leading causes of referral to mental health services in children and youths (Coghill, 2013). ODD is described by a frequent and persistent pattern of irritable and angry mood, vindictiveness, and inappropriate, negativistic, defiant, and disobedient behavior toward authorities, while CD is defined as a repetitive and persistent pattern of behavior, which violates the rights of others and major age-appropriate societal rules (American Psychiatric Association, 2013). With regard to comorbid disorders, DBD shows a specifically high overlap with ADHD. Estimates of comorbid ADHD, which vary from 35% to 50% of patients with DBD (Connor et al., 2010), point to a highly heterogeneous patient population. At a psychophysiological level, heart rate (HR), heart rate variability (HRV), and skin conductance (SC) are among the most

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frequently investigated biological markers of DBD. These measures reflect autonomic nervous system activity and general emotional arousal (e.g., Fanti, 2016). Looking at these measures more precisely, DBD seems to be associated with lower baseline HR and SC activity during resting state, as well as a lower reactivity to negative stimuli (Raine et al., 1990; Van Goozen et al., 2000). These findings imply a (psycho-)physiological hypo-arousal, resulting in patients seeking stimulating activities (Sensation seeking theory; Zuckerman, 2014), and not fearing the negative consequences of their actions (Fearlessness theory, Raine et al., 1990) which might increase the likelihood to engage in aggressive behavior. However, other studies on the physiological activity in DBD present contradictory and rather mixed findings, pointing to either lower or higher autonomic activity in DBD youth (Fanti et al., 2018). Further, a very recent meta-analysis, which analyzed 34 case-control studies, found no significant differences between typically developing peers (TD) and DBD for HR, but significant differences for task related SCR with a moderate effect size. Additionally, they found a significant negative association between baseline and task-related HR and conduct problems (Fanti et al., 2019).

Since the sum of empirical findings indicate strong heterogeneity of physiological patterns in patients diagnosed with DBD, there is a need to further disentangle the relationship between DBD and physiological indices taking into account different subtypes of aggression, particularly proactive (i.e. instrumental, goal-directed, unemotional, hypo-arousal) and reactive aggression (i.e. impulsive, emotional, hyper-arousal). There are only a few studies, which looked at subtype-specific differences: in a recent study from Schoorl et al. (2017), high HR and SCL were associated with reactive aggression, whereas low HR and low SCL were associated with proactive aggression in a clinical sample. Further, the new DSM-5 specifier for conduct disorder considers the level of callous-unemotional traits (i.e. lack of empathy, absence of guilt, shallow and deficient emotions), which might explain further variance within this heterogeneous disorder. Studies that analyzed the relationship between CU traits and psychophysiological measures found lower HR and SC being related to high CU traits in response to pain (Muñoz et al., 2007). The proactive subtype, together with high levels of CU traits represents an under-aroused aggression-related subtype, which might potentially be a mechanism related to higher engagement in aggression-related behaviors (Fanti et al., 2019). The latest fMRI study, which investigated the response to negative faces taking into account aggression subtypes, revealed that participants with high levels of CU showed reduced amygdala activity along with reduced SCR to negative faces (Aggensteiner et al., 2020).

In addition to HR and SC, electrophysiological measures such as the electroencephalogram (EEG) are rather underrepresented in aggression-related disorders. The few published studies found striking similarities to ADHD patients. As such, higher slow-wave activity most prominently in the theta frequency band, which is normally associated with ADHD, was found in delinquent children (Knyazev et al., 2002), and antisocial personality disorder (Lindberg et al., 2005). Furthermore, typically decreased beta activity in ADHD has been also found in antisocial participants (Gilmore et al., 2010). Taking together the findings for both disorders, there appears to be a link between ADHD and other forms of externalizing disorders. However, in both disorders, inconsistent results have been reported. For example, Clarke and colleagues speculated that higher levels of beta activity may define a particular subgroup of children with ADHD. This subgroup might be more hyper-aroused and possibly more hyperactive than other subgroups of ADHD (Clarke et al., 2001). Interestingly, similar results were reported in a sample of homicidal men (Lindberg et al., 2005). A recent meta-analysis of 62 studies tried to disentangle the literature of ADHD and aggression-related disorders: externalizing behaviors compared to ADHD showed a negative relationship between alpha power and antisocial behavior, and that exclusive slow-waves were particularly sensitive for ADHD, but not for antisocial or mixed samples (Rudo-Hutt, 2015). Nevertheless, preceding literature implies a large overlap between ADHD and other externalizing disorders. This is only slightly surprising, since there is a large overlap regarding the clinical phenotypes and considering the heterogeneous nature of these disorders.

Our study aimed to assess differences between TDs and youths with DBD with regard to peripheral measures (HR and SC) and neurophysiological measures (EEG) and to explore the relationship with the main DBD symptoms. Further, we explored if accounting for aggression-related subtypes or CU traits in children and adolescents with high aggression, can disentangle the mixed and contradictory findings on HR, SCR, and EEG. We expect differences in aggression-related subtypes with reduced HR and SCR for patients scoring high on proactive aggression and higher HR and SCR for participants with higher reactive aggression. With regard to EEG, we expect that alpha power is negatively related to aggression.

2. Methods and materials

2.1. Participants

Participants for the current analysis were recruited as part of the EU-Aggressotype and EU-MATRICS projects, conducted at two different sites (Mannheim and Zürich). In total, 74 participants aged 8–18 years were assessed. Cases were diagnosed with ODD and/or CD based on structured diagnostic interviews with child and parents using the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) (Kaufman et al., 1997) according to DSM-5, or scored above the clinical cut-off for aggressive behavior and/or rule-breaking behavior as measured with the Child Behavior Checklist completed by parents, teachers or youths (CBCL/TRF/YSR) (Achenbach et al., 1991). In the TD comparison group, no DSM axis I disorder, assessed via K-SADS, and no clinical score in the CBCL, TRF or YSR was allowed. Exclusion criteria for all participants were: IQ < 80 measured from four subtests (vocabulary, similarities, block design, and picture completion/matrix reasoning) of the Wechsler Intelligence Scale for Children-IV (Wechsler, 2003) or the WAIS-IV for participants older than 16 years, and a primary DSM-5 diagnosis of psychosis, bipolar disorder, major depression, and/or an anxiety disorder. For cases, medication had to be stable for at least two weeks prior to inclusion. Ethical approval for the study was obtained for all sites separately from local ethics committees. Written informed consent was given by the participants and their parents or legal representatives.

2.2. Questionnaires

The outcomes consisted of the following questionnaires: the Child and Behavior checklist (CBCL, Achenbach et al., 1991) with their subscales rule-breaking and aggression. The Inventory of Callous-Unemotional Traits (ICU) (Frick, 2004) rated by parents, and the self-reported Reactive and Proactive Questionnaire (Raine et al., 2006) were used for assessing CU traits and subtypes of aggression, respectively.

2.3. Psychophysiological recordings (HR and SC)

As depicted in Fig. 1, participants started with a three-minute resting state (white fixation cross) measurement (resting 1). Subsequently, emotional stimuli consisting of 18 pictures from the International Affective Picture System (IAPS; Lang et al., 2008), were presented in random order. Three different emotions were presented using 6 distinct pictures of negative, positive, and neutral valence. These stimuli have previously been validated in 8 to 13-year-old participants as well as in CD patients (Mueller et al., 2004). However, one extremely unpleasant picture (a dead woman's face covered in blood) was considered inappropriate for our study sample of children and adolescents. Therefore, the unpleasant picture was replaced by another IAPS picture of equal valence. Images were presented following a three-second fixation period prior to each stimulus. The randomly presented pictures appeared for 6 s

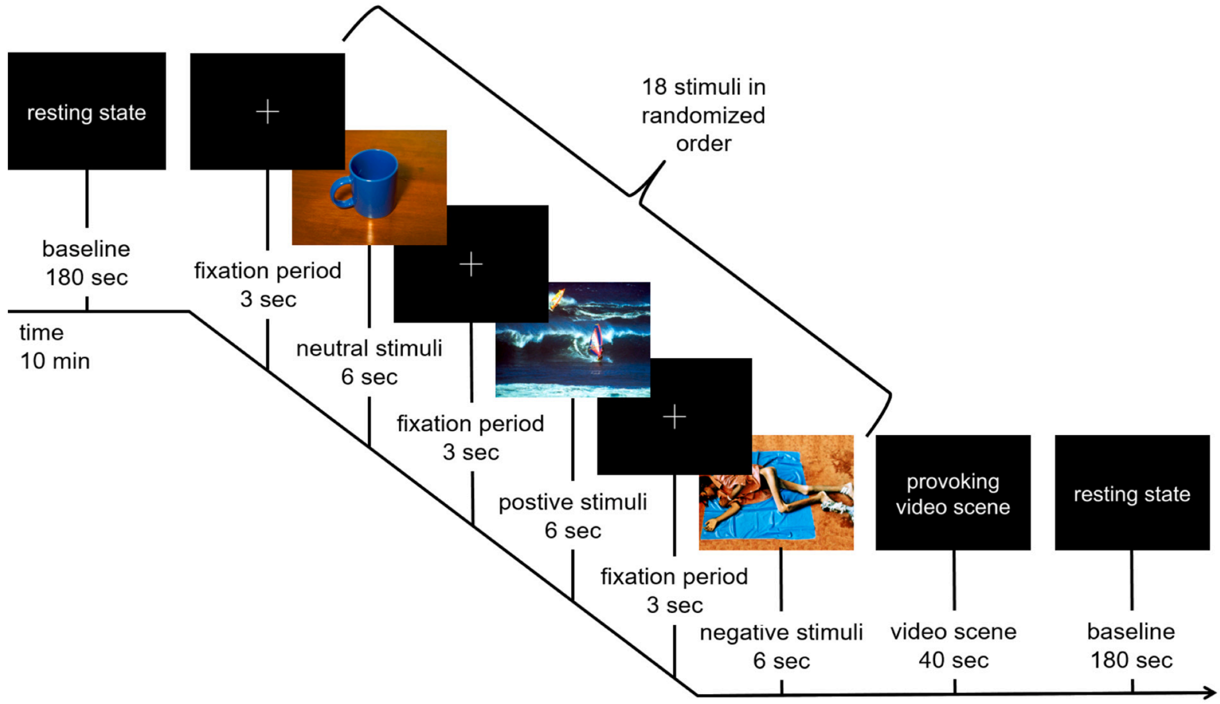

Fig. 1. The subtyping paradigm.
Recording started with a three-minute resting state (white fixation cross) measurement (resting 1). Subsequently, emotional stimuli consisting of 18 pictures from the International Affective Picture System (IAPS; Lang et al., 2008), were presented in random order. Three different emotions were presented using 6 distinct pictures of negative, positive, and neutral valence. After the emotional images, a provoking video sequence from first-person perspective was presented for 40 s. The experimental recording ended with a final resting state for 3 min, concurrent to the first resting state (resting 2).

each. After the emotional images, a provoking video sequence from first-person perspective was presented for 40 s. The experimental recording ended with a final resting state for 3 min, concurrent to the first resting state (resting 2). Altogether, the procedure (setup, performance, removal) lasted approximately 30 min, while data was recorded during 10 min (Fig. 2).

2.4. Electrophysiological recording and pre-processing

Skin conductance (SC), heart rate (HR), and neurophysiological data assessed via the electroencephalogram (EEG) were recorded. To assess psychophysiological data, the CE-certified 22-channel TheraPrax® Q-EEG-System (NeuroConn GmbH, Illmenau, Germany) was used. SC was recorded with Ag-AgCl electrodes on the third and fourth finger of the non-dominant hand, centered at the volar surface of the distal phalanges

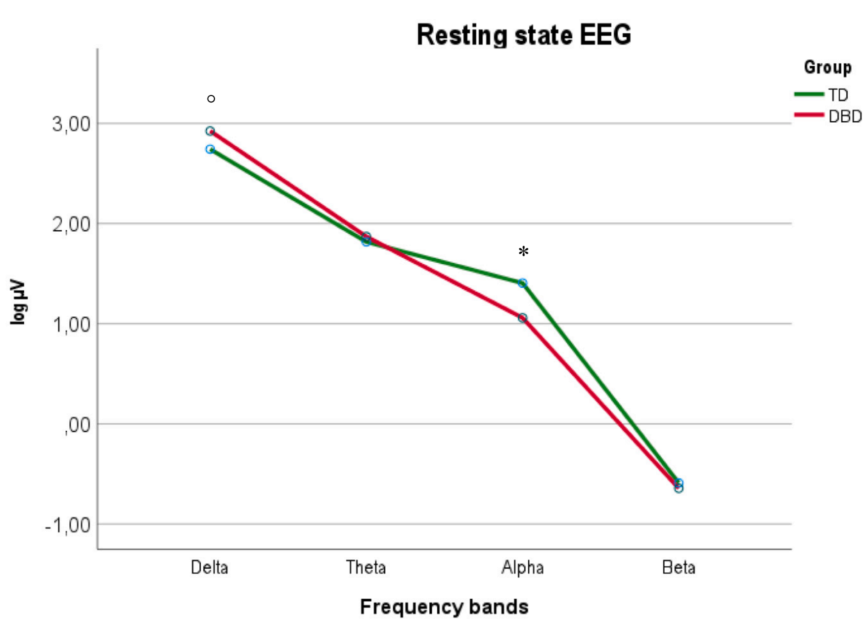

Fig. 2. Resting state EEG.
Frequency group interaction for resting state EEG measurements over all channels (Fz, Cz, Pz). °p < .1, *p < .05.

and filled with an SC electrolyte gel (TD-246 Electrode Paste, Discount Disposables, Vermont, USA). The room temperature was kept at a standardized level to prevent influences on SC. Due to a technical resolution limit of the Thera Prax system, only SC responses above a threshold of 1.9 μS were registered. Further, HR was tracked by applying a finger clip pulse oximeter sensor (Nonin Medical, Inc., Plymouth, USA) to the participant's second finger. Finally, Ag-AgCl electrodes for recording EEG (at electrode locations Pz, Cz, Fz; reference electrode on the left mastoid; ground electrode on the right mastoid) were set. The scalp electrode positions were prepared by swabbing the with medical ethanol and gently abraded with Nuprep skin preparation gel (Weaver and Company, Colorado, USA). The electrodes were fixated with Ten20 conductive EEG paste (Weaver and Company, Colorado, USA) on the participant's head. Impedances were kept below 20 kΩ. All psychophysiological signals were recorded with a sampling rate of 512 Hz. For EEG, a high-pass filter was set at 0.1 Hz and a low-pass filter at 500 Hz. Participants were instructed to sit as still as possible and an experienced technician visually monitored the measurements.

SC data were downsampled offline to 10 Hz and analyzed in Ledalab (Version 3.4.9; www.ledalab.de) applying continuous decomposition analysis (CDA). For further analysis, we extracted the time integral of the SCR (ISCR) (Benedek and Kaernbach, 2010). SCRs were defined as responses between 0.9 and 4 s after stimulus presentation that needed to exceed 0.01μS (Boucsein et al., 2012). The SCR amplitude was log-transformed by means of 1 + logSCR to obtain normally distributed data. HR and EEG data were analyzed using Brain Vision Analyzer 2.1 (Brain Products, Gliching, Germany). HR data were bandpass filtered with a low cutoff of 5 Hz and a high cutoff of 15 Hz. The R-waves time series were derived from the HR data by a semi-automatic solution of Brain Vision Analyzer and checked manually for missed or incorrect R-peak registration. Thereafter, the correctly recorded R-peaks were exported and heart rate and heart rate variability were calculated with an in-house MATLAB script. With regard to the EEG data, we bandpass filtered the signal (low cutoff 1 Hz and high cutoff 30 Hz, Notch 50 Hz). The data was re-referenced to the left mastoid. Artifact inspection was done semi-automatically (−200 μV to +200 μV) and the maximal allowed difference was set at 200 μV. EEG data was only analyzed for the resting state condition, because of the few repetitions of stimulus presentation and the therefore, low number of sweeps with regard to the emotional images. Epochs of the resting state condition were extracted for 2,5 s with a 50% overlap. Afterwards, data were again semi-automatically inspected for artifacts (exceeding −150 μV to +150 μV, maximal allowed difference was set at 100 μV). Fast Fourier transformation (FFT, Hanning window) was then applied to the remaining epochs and averaged. Participants with fewer than 20 epochs were excluded from the analyses. Finally, the frequency power was exported for the following frequency bands; delta (1.5 Hz to 3,5 Hz), theta (3,5 Hz to 7,5 Hz), alpha (7,5 Hz to 12,5 Hz), and beta (12,5 Hz to 30 Hz).

3. Statistical analysis

All statistical analyses were run in SPSS Version 25. Effect sizes following Cohens d were reported (Cohen, 1988).

3.1. Demographic data

Group differences in demographic variables were analyzed using analysis of variance (ANOVA) or Chi-square tests, when appropriate.

3.2. Resting state condition

SC, HR, and HRV were analyzed separately by a repeated measures (RM)-ANOVA with a between factor of group and a within factor of time (resting 1 and resting 2). EEG data were log transformed and analyzed by a RM-ANOVA with a between factor group and the within factors frequency (delta, theta, alpha, and beta), channels (Fz, Cz, and Pz) and time (resting 1 and resting 2). Additionally, all analyses were repeated including medication as a covariate.

3.3. Emotional pictures and video sequence

SCR, HR, and HRV data were analyzed separately by a RM-ANOVA with a between factor of group and the two within factors of emotion (negative, positive, and neutral) and condition (baseline and picture). The video sequence was analyzed by means of an ANOVA. Additionally, all analyses were repeated including medication as a covariate.

3.4. Stepwise regression analysis

To assess if aggression and its subtypes can be predicted by psychophysiological measurements, a stepwise linear regression models were applied. In a first step, IQ, age, sex and medication were added as control variables. In a second block, resting state psychophysiological measurements were introduced (SCL, HR, HRV) and in a third block we introduced the four EEG frequency power bands (delta, theta, alpha, and beta band).

4. Results

4.1. Demographic data

Table 1 shows the sample characteristics. From 74 participants who underwent the psychophysiological assessment, data from 11 participants had to be excluded due to missing data or technical problems during the recording. Finally, 63 participants were included for final analysis, 15 TDs and 48 cases. In total 18 participants were diagnosed with ODD, 26 with ODD+CD, one with only CD and three based on the CBCL cut-off. Both groups did not differ with regard to gender (p = .111), but the cases group had a lower IQ (p = .038). No significant between group differences were obtained for age (p = .194). Additionally, five participants in the cases group were left handed.

4.2. Resting state condition

4.2.1. Heart rate and heart rate variability

With regard to HR, RM-ANOVA showed significant higher heart rate in the cases group [$F(1,57) = 6.398$, $p = .014$, ES = 0.75]. Additionally, and independent of groups, heart rate was higher at resting 2, showing a significant effect of time [$F(1,57) = 13.643$, $p < .001$, ES = 0.22].

In analogy to the HR, HRV was significantly lower in the cases group [$F(1,57) = 5.144$, $p = .028$, ES = 0.66], and showed a significant effect of time [$F(1,57) = 9.682$, $p = .003$, ES = 0.38].

However, when including medication as a covariate, a main effect of medication emerged for HR [$F(1,56) = 6.240$, $p = .015$] and HRV [$F(1,56) = 6.455$, $p = .014$] which lead to non-significant group differences for HR [$F(1,56) = 1.682$, $p = .200$] and HRV [$F(1,56) = 1.130$, $p = .292$], indicating that higher HR and lower HRV were driven by the medication status of the participants.

4.2.2. Skin conductance level

For SC, RM-ANOVA showed neither significant differences between groups [$F(1,58) = 0.506$, $p = .480$, ES = 0.04], nor an effect of time [$F(1,58) = 0.806$, $p = .806$]. Including medication as a covariate did not influence the results.

4.2.2.1. Electroencephalogram. The EEG data showed a significant interaction between frequency power and group [$F(3,159) = 5.089$, $p = .002$]. Post-hoc comparisons showed significant lower alpha ($p = .043$, ES = −0.27) and a trend for higher delta frequencies in cases ($p = .096$, ES = 0.63). Furthermore, an interaction emerged for frequency and time [$F(3,159) = 3.784$, $p = .012$], showing that irrespective of group, lower

Table 1
Demographic data.

	TD			DBD				
	N	Mean	Std. Dev.	N	Mean	Std. Dev.	F	Sig.
Age	15	13.02	2.805	48	11.99	2.593	1.725	0.17
IQ	15	109.54	11.07	48	102.62	11.09	4.493	0.038
Sex m/f	15	66.7%/33.3%		48	85.4%/14.6%		X2 = 2.606	0.111
Medication	15	0.00%		48	43.80%		X2 = 9.844	0.001
CBCL								
Rule breaking	15	1.13	1.95	47	9.34	5.43	32.585	0.000
Aggression	15	1.67	2.82	47	19.83	5.95	129.208	0.000
ICU								
Callousness	15	3.8	3.7	47	9.89	5.29	17.107	0.000
Uncaring	15	13.47	4.22	47	16.57	4.91	4.785	0.033
Unemotional	15	5.87	2.85	47	6.32	3.38	0.218	0.642
ICU Total	15	23.87	7.86	47	34.19	9.52	14.422	0.000
RPQ								
Reactive	15	6.93	3.28	46	11.37	5.56	8.508	0.005
Proactive	15	1	1.69	46	4.24	5.09	5.804	0.019
Total	15	7.93	4.68	46	15.61	6.65	8.733	0.004

Note: CBCL, Child Behavior Checklist; ICU, Inventory of Callous-Unemotional Traits; RPQ, Reactive proactive Questionnaire; IQ estimated from a subset of the Wechsler Intelligence Scale for Children III; TD Typically developing peers; DBD, Disruptive behavior disorder. Different sample due to divergent missings in participants and questionnaires

frequencies, such as delta, were higher at resting 2 ($p < .001$), and a trend for theta ($p = .058$). Including medication as a covariate did not influence the significant interactions and strengthened the difference found in the alpha frequency band ($p = .029$), however, the trend level for delta frequency became non-significant ($p = .165$).

4.3. *Emotional reactivity*

4.3.1. *Heart rate and heart rate variability*

For HR, we only found a significant main effect of group indicating higher HR in cases [$F(1,59) = 4.436$, $p = .039$], and with regard to HRV we obtained the same effect with a trend for lower HRV in cases [$F(1,59) = 3.060$, $p = .085$]. During the video sequence, the same pattern emerged. Cases had a higher HR [$F(1,62) = 5.10$, $p = .27$] and a lower HRV [$F(1,62) = 4915$, $p = .30$]. Additionally, the video condition enhanced the HR in both groups considerably (by 36%). For details, see Table 2. As for resting-state data, HR and HRV are confound with medication. Including medication as a covariate resulted in no group differences for HR [$F(1,58) = 0.908$, $p = .345$] and HRV [$F(1,58) = 0.394$, $p = .532$].

4.3.2. *Skin conductance response*

No significant differences between groups were found for SC. Including medication as a covariate did not influence the results.

Table 2
Descriptive statistics of the subtyping paradigm.

Group		BPM	SD	HRV	SD	SCL/ SCR	SD
Resting 1	TD	74.07	7.66	0.82	0.09	6.75	4.37
	DBD	84.91	15.44	0.73	0.13	7.38	4.93
Neutral	TD	78.22	9.25	0.80	0.10	−0.69	1.60
	DBD	86.01	17.42	0.75	0.14	−0.62	1.35
Negative	TD	76.89	7.50	0.82	0.10	−0.59	1.69
	DBD	84.49	16.63	0.75	0.14	−0.32	1.32
Positive	TD	77.33	10.85	0.81	0.09	−0.55	1.70
	DBD	86.45	16.47	0.74	0.14	−0.35	1.38
Emotional Video sequence	TD	119.66	14.54	0.84	0.10	6.49	4.15
	DBD	136.14	25.59	0.75	0.13	7.38	5.56
Resting 2	TD	76.71	7.98	0.79	0.08	6.55	4.37
	DBD	86.64	15.34	0.72	0.13	7.83	5.96

Note: TD = typically developing peers. DBD = Disruptive behavior disorder. BPM = Beats per minute, HRV = Hear rate variability, SCR = Skin conductance response. SCL = Skin conductance level.

4.4. *Regression analyses*

Stepwise regression models revealed no significant effect for CBCL rule-breaking behavior and the peripheral measurements (SCL, HRV, and BPM, $R^2 = 0.109$, $p = .496$). Including EEG frequency band power increased the effect ($\Delta R2 = 0.212$, $p = .009$) and explained 32% of the variance, resulting in a significant main model ($p = .038$). More specifically, delta activity was positively related ($b = 0.326$, $p = .033$) and alpha activity negatively related ($b = -0.325$, $p = .033$). For details, see Table 3. For proactive aggression, the model with only SCL, HRV, and BPM revealed a trend ($R^2 = 0.189$, $p = .074$). However, without any significant prediction of SCL, HRV and BPM. Including EEG frequency band power had a significant additional impact for predicting proactive aggression ($\Delta R2 = 0.163$, $p = .024$). This model explained 35.2% of the variance ($p = .011$), where delta activity showed a positive association ($b = 0.401$, $p = .019$) and beta activity a negative association ($b = -0.444$, $p = .003$). No significant associations were found for reactive aggression or CU-traits. For details, see Table 4 and Fig. 3.

5. Discussion

The aim of our study was to evaluate the relationship between psychophysiological measurements (HR, HRV, SC, and EEG) and different measures of aggression-related behavior in patients with DBD and typically developing controls. Further, we assessed if focusing on different subtypes of aggression (CU traits, proactive, and reactive aggression) might disentangle the heterogenetic results obtained in previous studies for externalizing disorders. With regard to the psychophysiological measurements of arousal (HR, HRV, and SC), we found significant group differences for HR-measures with a higher HR, and a lower HRV in DBD when compared to the TD group, however this was mainly driven by medication. These findings are somewhat puzzling, since one previous study in DBD found higher HR and SCL with no impact of medication (Schoorl et al., 2015). Further, the latest meta-analysis on this topic did not include medication as a confounder (Fanti et al., 2019). Besides that it is well known that i.e. stimulants increases HR (Faraone, 2018). Additionally, we did not find any significant differences for SC, neither at baseline nor in response to emotional pictures. This finding differs from the results of a recent meta-analysis (Fanti et al., 2019) showing a moderate between-group effect for task-related SCR. We speculate that these diverging results, together with the absence of any subtype specific pattern on psychophysiological measurements, might be attributed to our experimental setup. It could

Table 3
Stepwise linear regression. CBCL Rule-breaking behavior.

Step	Predictor	Unstandardized coefficients		Standardized coefficients	t	p	2	F	p	ΔR2	
		B	Std. Error	β						p	
1	(Constant)	3.835	8.866		0.433	0.667	0.101	1.566	1.961		
	Age	0.524	0.290	0.233	1.805	0.076					
	IQ	−0.051	0.070	−0.096	−0.735	0.465					
	Sex	2.483	2.015	0.160	1.232	0.223					
	Medication	1.235	1.649	0.097	0.749	0.457					
2	(Constant)	−5.947	17.179		−0.346	0.731	0.109	0.924	0.496	−0.009	0.921
	Age	0.524	0.322	0.233	1.628	0.109					
	IQ	−0.051	0.073	−0.097	−0.699	0.487					
	Sex	2.506	2.148	0.162	1.167	0.249					
	Medication	1.430	1.886	0.113	0.758	0.452					
	SCL	−0.009	0.195	−0.006	−0.046	0.964					
	BPM	0.052	0.091	0.123	0.574	0.568					
	HRV	7.232	10.617	0.145	0.681	0.499					
3	(Constant)	−19.340	16.429		−1.177	0.245	0.321	2.105	**0.038**	0.212	**0.009**
	Age	0.994	0.382	0.442	2.601	**0.012**					
	IQ	−0.090	0.070	−0.170	−1.287	0.204					
	Sex	2.078	2.004	0.134	1.037	0.305					
	Medication	0.471	1.782	0.037	0.264	0.793					
	SCL	0.018	0.180	0.013	0.101	0.920					
	BPM	0.128	0.085	0.302	1.496	0.141					
	HRV	13.595	9.866	0.273	1.378	0.174					
	Delta	0.227	0.103	0.361	2.198	**0.033**					
	Theta	0.395	0.334	0.228	1.182	0.243					
	Alpha	−0.871	0.398	−0.325	−2.189	**0.033**					
	Beta	−4.892	2.818	−0.257	−1.736	0.089					

Note: SCL = Skin conductance level; BPM = Beats per minute; HRV=Heart rate variability. Significant effects are highlighted in bold

Table 4
Stepwise linear regression. Proactive aggression.

Step	Predictor	Unstandardized Coefficients		Standardized Coefficients	t	p	R^2	F	p	ΔR^2	
		B	Std. error	β							p
1	(Constant)	11.628	6.794		1.711	0.093	0.135	2.148	0.087		
	Age	−0.058	0.231	−0.032	−0.250	0.804					
	IQ	−0.095	0.055	−0.226	−1.724	0.090					
	Sex	2.666	1.501	0.228	1.777	0.081					
	Medication	0.982	1.308	0.099	0.751	0.456					
2	(Constant)	17.653	12.801		1.379	0.174	0.205	1.912	0.086	0.098	0.221
	Age	0.111	0.246	0.062	0.451	0.654					
	IQ	−0.110	0.056	−0.262	−1.966	0.055					
	Sex	2.851	1.560	0.244	1.827	0.073					
	Medication	−0.520	1.483	−0.052	−0.350	0.727					
	SCL	0.150	0.146	0.138	1.023	0.311					
	BPM	0.004	0.067	0.012	0.058	0.954					
	HRV	−10.189	7.879	−0.271	−1.293	0.202					
3	(Constant)	11.066	12.466		0.888	0.379	0.363	2.491	**0.015**	0.218	**0.028**
	Age	0.249	0.290	0.139	0.857	0.396					
	IQ	−0.125	0.054	−0.299	−2.320	**0.025**					
	Sex	2.856	1.496	0.244	1.909	0.062					
	Medication	−1.286	1.432	−0.130	−0.898	0.373					
	SCL	0.128	0.139	0.118	0.923	0.361					
	BPM	0.032	0.063	0.101	0.501	0.618					
	HRV	−5.258	7.513	−0.140	−0.700	0.487					
	Delta	0.415	0.300	0.198	1.383	**0.016**					
	Theta	−6.467	2.174	−0.432	−2.974	0.616					
	Alpha	−0.130	0.257	−0.092	−0.505	0.173					
	Beta	0.204	0.082	0.414	2.497	**0.005**					

Note: SCL = Skin conductance level; BPM = Beats per minute; HRV=Heart rate variability. Significant effects are highlighted in bold

be that case-control differences are more prominent in more stressful or realistic setups. In our own fMRI study, we had found that SCR were correlated negatively with CU-traits (Aggensteiner et al., 2020), however in our current laboratory setup which was without fMRI, we did not obtain the same results for SCR. In line with the conclusions of the recent meta-analysis (Fanti et al., 2019), the experimental paradigms used in psychophysiological research might not represent ecologically valid assessments of arousal and stress, underlining the need for incorporating new techniques, such as virtual reality settings or real-time monitoring.

Interestingly, we found more encouraging results with regard to the EEG measurement. Here, we identified a significant interaction effect between groups and EEG activity, with lower alpha activity in DBD, even after controlling for medication. These results are in line with the meta-analysis from Rudo-Hutt's (2015), which is - at least to our knowledge – the only one addressing EEG-studies in DBD.

Our regression analysis showed significant associations between theta and alpha band activity with dimensional measurements of rule-breaking behavior and delta and beta band activity with proactive

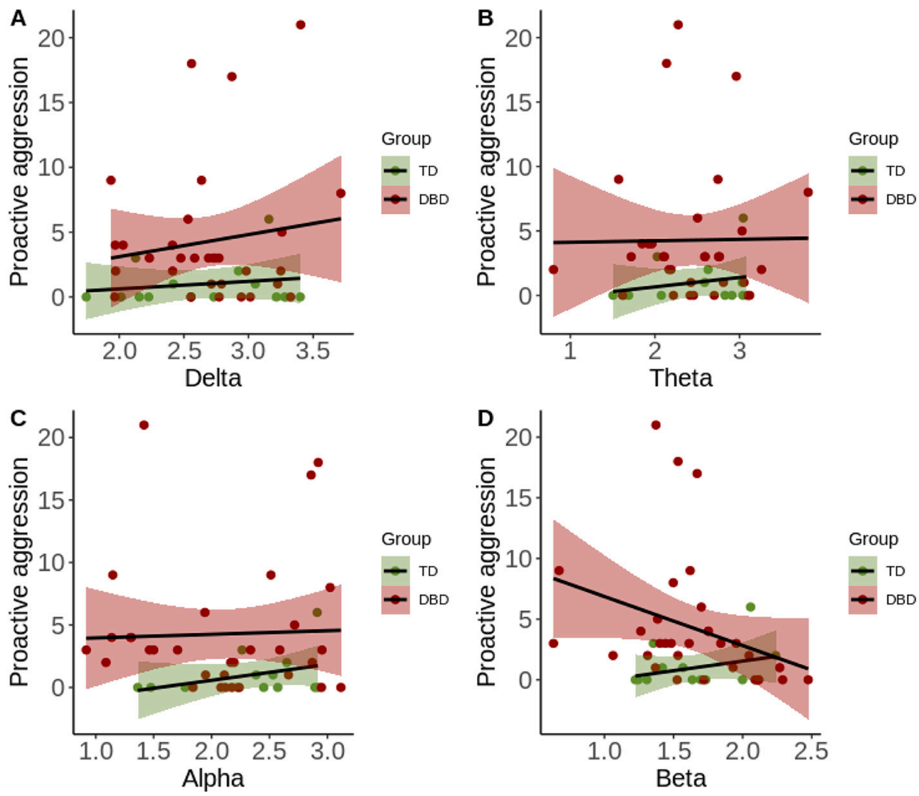

Fig. 3. EEG frequency power and proactive aggression.
Associations between Proactive aggression and spectral power (log transformed). A for Delta band, B for Theta band, C for Alpha band and D for Beta band. Delta activity showed a positive association ($b = 0.661$, $p = .012$) and beta activity a negative association ($b = -0.377$, $p = .018$).

aggression. Interestingly, the different indices of subtypes of aggression (RA, PA or CU traits) did not show any significant association with peripheral measurements (HR and SC). Only EEG assessment (high delta and reduced beta) showed a significant association with proactive aggression. This finding is in line with reduced beta frequency band power in antisocial behavior reported in previous studies (Gilmore et al., 2010; Houston and Stanford, 2005). Additionally, in a study by Clarke and colleagues, the authors speculated that higher levels of beta activity might define a subgroup of children with ADHD who are hyper-aroused and possibly more hyperactive and impulsive (Clarke et al., 2001). However, in a subsequent study, they showed that ADHD children with higher levels of beta had reduced SCL, suggesting that those participants were not hyper-aroused (Clarke et al., 2013). Furthermore, it has repeatedly been shown, that eyes closed alpha activity is negatively related to SCL (Barry et al., 2009; Barry et al., 2020), but this effect seem to be more robust for eyes closed condition or for alpha reactivity between eyes close to eyes open in comparison to an eyes open resting state measurement. Additionally, newer methods which applies principal component analysis (i.e. for alpha), might improve the understanding between arousal and resting state EEG measurements (Barry et al., 2020). So far, it thus remains unclear if those reported psychophysiological correlates of arousal consistently deviate in clinical samples or subgroups, warranting therefore more studies.

5.1. Limitations

As a limitation, we have to consider that our case-control comparison is only based on a small control group, and should therefore be interpreted with caution. Further, our experimental setup to assess emotional reactivity is based on only six repetitions per emotions, what probably might not be sufficient to induce high emotional reactivity that later are reflected in group differences or associations with aggression-related subtypes and behaviors. We further think that inclusion of a combined SCL, HR and EEG measurement during an eyes closed condition as an additional arousal manipulation (Barry et al., 2020) would have been an advantage and should be included in future work.

6. Conclusion

Taking together our findings, we found that EEG activity at rest might be more sensitive to detect group differences between DBD patients and typically developing controls than peripheral measurements, such as SC, HR or HRV. Additionally, specific associations between delta and beta band activity with proactive aggression were found, which might suggest a hypo-arousal related to this subtype of aggression. Whereas reduced alpha band activity was related to a more general aggression scores, since it did not show any relationship with specific aggression-related subtypes.

6.1. Disclaimer

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