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SHORT COMMUNICATION

Lower levels of cannabinoid 1 receptor mRNA in female eating disorder patients: Association with wrist cutting as impulsive self-injurious behavior

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Summary The cannabinoid 1 (CB 1) receptor as the primary mediator of the endocannabinoid (EC) system was found to play a role in eating disorders (EDs), depression, anxiety, and suicidal behavior. The CB 1 receptor is assumed to play a crucial role in the central reward circuitry with impact on body weight and personality traits like novelty-seeking behavior. In a previous study we found higher levels of CB 1 receptor mRNA in patients with anorexia nervosa (AN) and bulimia nervosa (BN) compared to healthy control women (HCW). The aim of the present study was to investigate the possible influence of the EC and the CB 1 receptor system on wrist cutting as self-injurious behavior (SIB) in women with EDs ($n = 43$; AN: $n = 20$; BN: $n = 23$). Nine ED patients with repetitive wrist cutting (AN, $n = 4$; BN, $n = 5$) were compared to 34 ED patients without wrist cutting and 26 HCW. Levels of CB 1 receptor mRNA were determined in peripheral blood samples using quantitative real-time PCR. ED patients with self-injurious wrist cutting exhibited significantly lower CB 1 receptor mRNA levels compared with ED patients without wrist cutting and HCW. No significant differences were found between ED patients without a history of wrist cutting and HCW. Furthermore, a negative association was detected between CB 1 receptor mRNA levels and Beck Depression Inventory (BDI) scores. To our knowledge, this is the first study reporting a down-regulation of CB 1 receptor mRNA in patients with EDs and wrist cutting as SIB. Due to the small sample size, our results should be regarded as preliminary and further studies are warranted to reveal the underlying mechanisms.

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1. Introduction

The endocannabinoid (EC) system with cannabinoid (CB) receptors (CB 1/CB 2) and their endogenous ligands N-arachidonoyl ethanolamide (AEA) and 2-arachidonoylglycerol (2-AG) is involved in brain reward processes and the regulation of appetite and energy intake. As opposed to other neurotransmitters, endocannabinoids are synthesized and released 'on demand'. CB 1 receptors modulate orexigenic vs. anorexigenic effects through shaping either the glutamatergic or the GABAergic neurotransmission in the brain. These modulatory effects of endocannabinoids at CB 1 receptors are assumed to be dose dependent (Bellocchio et al., 2010). CB 1 receptor antagonists like rimonabant were developed as anti-obesity drugs but were found to induce central side effects such as depression- and anxiety and were thus withdrawn from the market. With respect to personality traits, CB 1 receptor availability was found to be inversely related to high novelty-seeking personality, which primarily affects action impulsivity (Van Laere et al., 2009).

The results regarding suicide, novelty-seeking personality and our previous findings of significantly higher levels of CB 1 receptor mRNA levels in patients with EDs (Frieling et al., 2009) raised the question if repetitive, impulsive self-injurious behavior (SIB) like wrist cutting is associated with a modified function of the EC system. SIBs encompassing self inflicted body injuries most frequently by scratching and cutting to hands and arms are known to be highly prevalent in ED patients across diagnostic subgroups reaching a life time prevalence of more than 34% (Paul et al., 2002). Besides its impact on affect regulation, the modulatory EC and CB 1 receptor systems are well known to influence pain processing leading to analgesic effects (Sagar et al., 2009), which might further enhance the susceptibility for self inflicted skin injuries. Although we previously found an up-regulation of CB 1 receptor mRNA among both AN and BN patients, the more severely impaired patients as assessed with the German version of the Eating Disorder Inventory 2 (EDI-2) showed lower levels of CB 1 expression. Hence, there was a negative correlation between severity of the ED and CB 1 expression. As perfectionism and impulsivity play particular roles in the clinical course of EDs and higher impulsivity influences the susceptibility for wrist cutting as an impulsive SIB, we conducted an explorative analysis within the previously described sample of ED patients regarding this possible link (Frieling et al., 2009). We expected to find evidence for an alteration of the EC system in patients with histories of self-injurious wrist cutting. We focused on CB 1 receptor mRNA measurements in peripheral blood samples. Due to the small sample size of patients with ED and SIB, we combined patients with AN and BN and compared them to healthy control subjects.

2. Methods

This analysis was part of a larger study on EDs (HEaD), which was approved by the local Ethics Committee of the University of Muenster, Germany. All participants gave their written informed consent. ED diagnoses were made according to DSM-IV criteria. Twenty patients met criteria for AN and 23 for BN. Neither had AN patients a previous history of BN nor had BN patients a prior history of AN. The severity of the ED symptomatology was assessed by using the German version of the Eating Disorder Inventory 2 (EDI-2) (Frieling et al., 2009). Histories of wrist cutting were determined from interviews as a dichotomous yes/no variable. Patients and HCW were asked if they had repeatedly injured themselves or are still engaged in self-injury through skin-cutting at their wrists. Nine patients (AN: 4/20; BN: 5/23) affirmed, HCW negated this question. The presence of episodes of uncontrollable overeating (binging) and/or purging behaviors (e.g. self-induced vomiting, vigorous physical exercise) were determined by patient interviews. In addition, the severity of depressive symptoms was assessed by using the Beck Depression Inventory (BDI) and the presence of a co-morbid borderline personality disorder (BPD) was assessed using the SCID-II interview performed by a senior psychiatrist. In the 26 age matched HCW, psychiatric co-morbidity was ruled out using the SCID-I interview.

Table 1 Demographic data.

	Wrist cutting		No wrist cutting		HCW (n = 26)	F/T	df	P
	Anorexia (n = 4)	Bulimia (n = 5)	Anorexia (n = 16)	Bulimia (n = 18)				
Age [years]	25.25 (13.2)	26.80 (11.4)	26.69 (10.3)	25.67 (7.0)	26.27 (7.66)	0.002	2	0.99
BMI [kg/m^2]	17.35 (1.2)	21.82 (1.5)	15.50 (2.0)	22.66 (2.9)	20.88 (1.59)	1.637	2	0.20
Years of illness [years]	11.75 (11.5)	8.00 (7.7)	9.20 (11.0)	9.33 (5.6)		−0.124	41	0.902
Comorbid BPD [n]	1	1	1	1				0.054
BDI score	24.33 (10.6)	28.00 (8.2)	21.63 (9.9)	16.83 (7.9)		−2.135	41	0.039*
Presence of binging behavior	2	4	6	13				0.99
Presence of purging behavior	4	5	10	14				0.089

Demographic data of the study population. Group differences were tested either with one-way ANOVA (Age and BMI), t-tests (BDI, years of illness) or Fisher's exact test.

* Significant between group differences. BDI: Beck's Depression Inventory; AN: anorexia nervosa; BN: bulimia nervosa; BPD: borderline personality disorder; HCW: healthy control women.