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Affective reactivity in heroin-dependent patients with antisocial personality disorder

Marc Walter [a,*], Bigna Degen [a,b], Constanze Treugut [a], Jürgen Albrich [a,b], Monika Oppel [a,b], André Schulz [c], Hartmut Schächinger [b,c], Kenneth M. Dürsteler-MacFarland [a,d], Gerhard A. Wiesbeck [a]

[a] Psychiatric Hospital, Division of Substance Use Disorders, University of Basel, Switzerland
[b] Department of Psychology, University of Basel, Switzerland
[c] Institute of Psychobiology, Department of Clinical Physiology, University of Trier, Germany
[d] Psychiatric Hospital, Division of Substance Use Disorders, University of Zurich, Switzerland

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ABSTRACT

The Antisocial personality disorder (ASPD), one of the most common co-morbid psychiatric disorders in heroin-dependent patients, is associated with a lack of affective modulation. The present study aimed to compare the affect-modulated startle responses of opioid-maintained heroin-dependent patients with and without ASPD relative to those of healthy controls. Sixty participants (20 heroin-dependent patients with ASPD, 20 heroin-dependent patients without ASPD, 20 healthy controls) were investigated in an affect-modulated startle experiment. Participants viewed neutral, pleasant, unpleasant, and drug-related stimuli while eye-blink responses to randomly delivered startling noises were recorded continuously. Both groups of heroin-dependent patients exhibited significantly smaller startle responses (raw values) than healthy controls. However, they showed a normal affective modulation: higher startle responses to unpleasant, lower startle responses to pleasant stimuli and no difference to drug-related stimuli compared to neutral stimuli. These findings indicate a normally modulated affective reactivity in heroin-dependent patients with ASPD.

1. Introduction

Heroin dependence is a chronic relapsing brain disorder that is characterized by an overwhelming compulsion to seek and use heroin, despite negative consequences (Leshner, 1997). It is well known that opioid maintenance treatment produces favorable treatment retention and outcome in heroin-dependent patients (Kreek and Vocci, 2002; Kreek et al., 2002; Strain and Stitzer, 2006). However, some heroin-dependent patients do not respond adequately to treatment, but continue to use heroin. Neuropsychological consequences associated with heroin use are common. In particular, impulse control dysfunction and negative affective states have been described (Koob and LeMoal, 1997; Swann et al., 2002).

Antisocial personality disorder (ASPD) is a commonly diagnosed serious health mental disorder in substance users, with approximately 16–27% meeting DSM-IV criteria suffering from ASPD (Alterman and Cacciola, 1991; Morgenstern et al., 1997; Verheul, 2001; Goldstein et al., 2007). Psychopathological symptoms such as impulsive-aggressive behavior, irresponsibility, egocentricity, lack of conscience, and social maladjustment are features of ASPD (Martens, 2001). It is important to note that ASPD has been criticized for overly relying on antisocial behaviors, while excluding many of the affective and interpersonal characteristics to be central to the construct of psychopathy such as affective shallowness and the lack of empathy (Kiehl, 2006). Nevertheless, there is a wide clinical overlap between ASPD and psychopathy. In general, ASPD has been associated with a poor treatment outcome, inadequate psychosocial functioning, patterns of more problematic substance use, and deficits in emotional processing (Galen et al., 2000; Birbaumer et al., 2005).

Both ASPD and heroin dependence are associated with a hypoactivity of brain regions involved in emotional processing. One of the cortical, limbic, and paralimbic regions that have been implicated in emotional processing is the amygdala (Phan et al., 2002). Animal experiments have shown that the amygdala functioning is essential for the acquisition of fear conditioning and the magnitude of the startle reflex (Antoniadis et al., 2009). The startle reflex paradigm represents a valid measure of general affective processing, known to be enhanced during negative emotion (Grillon et al., 2007; Jovanovic et al., 2009). It is reliably elicited by unexpected, intense external stimuli such as a sudden, loud noise (Lang et al., 1990; Turpin et al., 1999; Schulz et al., 2009). Acute withdrawal from opioids potentiates the startle response which may reflect a withdrawal-induced anxiety-like state of the organism (Harris and Gewirtz, 2004). Healthy individuals show a significant linear relationship between affective valence and startle magnitude, with response strength increasing from pleasant to neutral to unpleasant stimuli (Vrana et al., 1988; Hamm et al., 1993; Patrick et al., 1993). In

* Corresponding author. Psychiatric Hospital of the University of Basel, Wilhelm Klein-Str. 27, CH-4025 Basel, Switzerland. Tel.: +41 61 325 5112; fax: +41 61 325 5583.
E-mail address: marc.walter@upkbs.ch (M. Walter).

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heroin-dependent patients the increased startle response to pleasant stimuli compared to controls were seen as the inhibited responding to natural rewards (i.e. anhedonia) (Lubman et al., 2009).

Antisocial and psychopathic individuals fail to exhibit a normal affective modulation of startle responses to different affective stimuli because they did not show significant differences from pleasant to neutral to unpleasant stimuli (Patrick et al., 1993; Herpertz et al., 2001; Pastor et al., 2003). ASPD patients with alcohol dependence also demonstrate a lack of affective startle modulation (Miranda et al., 2003). This lack of emotional modulation to affective stimuli in individuals with ASPD putatively reflects a general deficit in the perception and processing of affective information (Levenston et al., 2000; Herpertz et al., 2001) which may negatively affect their treatment. It remains unclear whether the attenuated affective reactivity in heroin dependence results from the common co-occurring ASPD traits or from regular opioid intake (Koob and LeMoal, 1997; Baker et al., 2004).

However, the affect-modulated startle reflex has not yet been investigated in heroin-dependent patients with and without co-occurring ASPD. Thus, it is not clear whether the co-occurring ASPD is associated with a lack of affective modulation to emotional stimuli and drug cues or has no significant influence on the affective modulation in heroin-dependent patients. The present study aimed to examine the affect-modulated startle response in heroin-dependent patients with co-occurring ASPD as compared to those without ASPD and to healthy individuals. A priori we have expected that heroin-dependent opioid-maintained patients would show an increased startle magnitude to pleasant stimuli, a decreased startle magnitude to drug-related stimuli compared to healthy controls, and an impaired affective modulation during all affective stimuli for heroin-dependent patients with co-occurring ASPD as compared to those without ASPD and to healthy controls.

2. Methods and materials

2.1. Participants

Table 1 summarizes the sociodemographic and diagnostic characteristics of the sample. The heroin-dependent patient group comprised 20 opioid-maintained individuals with co-occurring ASPD, aged 20–55 years, and 20 opioid-maintained individuals without co-occurring ASPD, aged 28–48 years. They were recruited from the methadone maintenance clinic and from the center for heroin (diacetylmorphine) prescription of the Psychiatric Hospital of Basel, Switzerland. The healthy control group consisted of 20 healthy participants from the general population who were recruited by advertisement. The three groups were controlled for sex, age and the proportion of smokers. Exclusion criteria for all participants included a positive breath-alcohol test, a history of hearing problems, tinnitus, a history of significant medical problems or major mental disorders (other than substance use disorders for heroin-dependent participants), or medication with a known impact on the physiological response measures (e.g. benzodiazepines). The local ethics committee approved the study protocol. All participants signed written informed consent and received gift vouchers as compensation.

Table 1
Sociodemographic and diagnostic characteristics of the study sample.

Measures	HD + ASPD	HD-ASPD	HC
	($n=20$)	($n=20$)	($n=20$)
	Mean (S.D.)	Mean (S.D.)	Mean (S.D.)
Age (S.D.)	35.6 (7.3)	38.7 (5.5)	35.6 (8.6)
Male gender (%)	18 (90.0)	16 (80.0)	16 (80.0)
Daily methadone dose (in mg)	86 (72.4)	90 (58.0)	–
Daily DAM dose (in mg)	330 (273.7)	310 (165.9)	–
Age of HD onset (years)	19.0 (4.5)	19.0 (5.0)	–
Duration of HD (years)	14.9 (8.2)	14.9 (6.8)	–
Number of ASPD criteria	3.5 (0.8)	1.5 (0.5)***	0.0 (0.0)
Impulsivity Score, BIS	1.55 (0.48)	1.66 (0.43)	2.02 (0.41)
Novelty seeking, TPQ	21.42 (14.37)	17.95 (12.54)	16.22 (4.74)
Harm avoidance, TPQ	20.79 (26.33)	15.16 (13.29)	13.47 (5.20)
Reward dependence, TPQ	18.00 (4.89)	16.63 (7.80)	16.63 (3.62)
Smokers (%)	17 (85.0)	17 (85.0)	17 (85.0)
Heroin-maintained patients (%)	10 (50.0)	10 (50.0)	–

HD = Heroin dependence; ASPD = Antisocial personality disorder; DAM = Diacetylmorphine; HC = healthy controls.
There were no other significant differences on any comparison between HD + ASPD, HD-ASPD, or HC.
*** = $p<0.001$.

2.2. Picture material

For neutral, pleasant, and unpleasant stimuli a set of 72 photographs was chosen from the International Affective Picture System (IAPS; Lang et al., 1997). Pleasant pictures displayed cubs, babies, and people doing sports and nude scenes. Unpleasant pictures showed mutilated bodies, acquired immune deficiency syndrome (AIDS) victims, car crashes, tornados, and weapons. Neutral pictures included household objects and neutral sceneries. As the IAPS only comprises three drug-related pictures, the remaining 21 color pictures consisted of self-taken digital photographs from the research team's assemblage. They depicted scenes of heroin use, paraphernalia, places associated with heroin use and scenes of unidentified persons cooking up and injecting heroin. The IAPS identification numbers for the pleasant pictures are: 1440, 1710, 1999, 2070, 2092, 2655, 4180, 4255, 4601, 4599, 4235, 4300, 4310, 4531, 4561, 4659, 4660, 4664, 4680, 7502, 8200, 8465, 8490, 8496. Mean valence: 6.82 (S.D.: 1.81), mean arousal: 5.41 (S.D.: 2.41). The identification numbers for the unpleasant pictures are: 1300, 2900, 3030, 3051, 3140, 3150, 3220, 3230, 3550, 5970, 5971, 6300, 6370, 6570, 6940, 9042, 9080, 9570, 9910, 9181, 9120, 9300, 9920, and 9921. Mean valence: 2.63 (S.D.: 1.60), mean arousal: 5.92 (S.D.: 2.15). The identification numbers for the neutral pictures are: 2880, 7002, 7009, 7010, 7020, 7040, 7050, 7060, 7090, 7100 7233, 7705, 7211, 7217, 7175, 7820, 7830, 7235, 7187, 7186, 7150, 7160, 7205, and 7185. Mean valence: 4.98 (S.D.: 1.19), mean arousal: 2.86 (S.D.: 1.91). The pictures were scanned into a computer and resized to the same dimensions (90 mm high × 100 mm wide). All pictures were presented on a Pentium-IV class PC connected to a 17-inch Samsung SyncMaster color monitor.

2.3. Interviews and self-report measures

Clinically experienced interviewers trained to pay particular attention to distinguishing Axis I mental state conditions from Axis II personality trait phenomena interviewed all participants with the German version of the Structured Clinical Interview for Axis II disorders (SCID-II; Wittchen et al., 1997). Participants underwent testing for basic self-report measures of personality. The 30-item *Barratt Impulsivity Scale-11* (BIS-11; Barratt and Patton, 1983) was used to measure impulsivity. The 100-item *Tridimensional Personality Questionnaire* (TPQ; Cloninger, 1987) assessed the personality dimensions of novelty seeking, harm avoidance, and reward dependence. Both instruments have proven to be highly valid and reliable.

2.4. Startle eye-blink response

The eye-blink component of the acoustic startle reflex was measured by using an electromyographic startle system (Myoscan Pro, Thought Technology Ltd., Montreal, Can). The startle reflex was elicited by the computer-based software E-Prime (E-Prime, Psychology Software Tools, Inc., Forest Hills, Pa) running on a Pentium-IV class PC. All startle responses were recorded on a Compaq laptop using DASYLab8 software (DASYLab, National Instruments Ireland Resources Ltd.), with a sample rate of 1000 Hz and 16-bit A/D conversion. We assessed the eye-blink response as the peak electromyography (EMG) activity of the left musculus orbicularis oculi, using two solid gel Ag–AgCl one-way electrodes placed below the left eye with an interelectrode distance of 2 cm. A third (reference) electrode was taped on the abdomen. Amplified EMG (EMG MyoScan Pro, Thought Technology Ltd., Montreal, Canada, 0–400 μV, filter setting: narrow) was recorded with DasyLab 8.00.04 software (National Instruments Ireland Resources Ltd.) at a sampling rate of 1000 Hz, with a hardware based 50 Hz notch filter and band-pass filtered between 20 and 500 Hz. Data were then rectified and integrated with a time constant of 10 ms. The startle response was defined as the difference in amplitude between the baseline and the peak of response occurring during a time window of 20–150 ms after startle onset.

Signals with electrical and physiological artefacts, such as coinciding blinks or other facial muscular activities, which introduced noise to the baseline period and made the correct quantification of the response impossible were defined as missing and rejected from analysis. If responses were not visible (zero amplitude) at the typical response latency of a particular participant, response amplitude was set to zero. Zero response data were included in the averaging procedure, with startle response magnitude as the final output measure (Blumenthal et al., 2005). Preprobe baselines of the startle consisted of a burst of white noise with an intensity of 105 dB and a duration of 50 ms, the random interstimulus interval lasting between 2 and 5 s.

2.5. Study procedure

The participants underwent a 3-hour experiment, consisting of a standardized baseline assessment as well as a startle session consisting of a series of computer-based startle trials. Sessions began between 8:00–10:00 a.m. and took place in a separate, adequately illuminated laboratory room with a consistent level of sound, heat, and