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Dysregulated responses to emotions among abstinent heroin users: Correlation with childhood neglect and addiction severity☆

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ABSTRACT

The aim of this paper was to investigate the subjective responses of abstinent heroin users to both neutral and negative stimuli and the related hypothalamus-pituitary-adrenal reactions to emotional experience in relationship to their perception of childhood adverse experiences. Thirty male abstinent heroin dependents were included in the study. Emotional responses and childhood neglect perception were measured utilizing the State-Trait Anxiety Inventory Y-1 and the Child Experience of Care and Abuse Questionnaire. Neutral and unpleasant pictures selected from the International Affective Picture System and the Self-Assessment Manikin procedure have been used to determine ratings of pleasure and arousal. These ratings were compared with normative values obtained from healthy volunteers used as control. Blood samples were collected before and after the experimental sessions to determine both adrenocorticotropic hormone and cortisol plasma levels. Basal anxiety scores, cortisol and adrenocorticotropic hormone levels were higher in abstinent heroin users than in controls. Tests showed that anxiety scores did not change in controls after the vision of neutral slides, whilst they did in abstinent heroin addicts, increasing significantly; and increased less significantly after the unpleasant task, in comparison to controls. Abstinent heroin users showed significantly higher levels of parent antipathy and childhood emotional neglect perception than controls for both the father and the mother. Plasma adrenocorticotropic hormone and cortisol levels did not significantly increase after unpleasant slide set viewing among addicted individuals, because of the significantly higher basal levels characterizing the addicted subjects in comparison with controls. Multiple regression correlation showed a significant relationship between childhood neglect perception, arousal reaction, impaired hypothalamus-pituitary-adrenal axis response and addiction severity. Early adverse experiences seem to affect the entire interaction between hyper-arousal, reduced hormonal response to stress and addiction severity. Our findings, although obtained in a small number of subjects, indicate a significant link between the perception of parental style/care/support during childhood and the ability to cope with stressful emotional stimuli in adulthood and addiction severity.

1. Introduction

Evidence indicates that detoxified abstinent opioid users have shown compromised emotional response to natural reinforcing stimuli and reduced reward perception (Kornreich et al., 2003). Moreover, current opioid users also may have abnormal emotion processing when exposed to competent positive and negative stimuli (de Arcos et al., 2008). Nevertheless, there are few studies on the addicted patients' capacity to cope with emotions in general. With regard to emotional experience, in our previous study (Gerra et al., 2003), abstinent heroin users have been found to present increased arousal and emotional response to neutral images and reduced response to both pleasant and unpleasant images. More recently, current heroin

Abbreviations: HPA, hypothalamus-pituitary-adrenal; ACTH, adrenocorticotropic hormone; STAI, State-Trait Anxiety Inventory; CECA-Q, Child Experience of Care and Abuse Questionnaire; SAM, Self-Assessment Manikin; DSM, Diagnostic and Statistical Manual of Mental Disorders; SCI, Structural Clinical Interview; SIDP-IV, Structured Interview for DSM IV Personality Disorders-IV; IAPS, International Affective Picture System; GEE, Generalized Estimating Equation; ASI, Addiction Severity Index; CRF, corticotrophin releasing factor.

☆ The views expressed herein are those of the author(s) and do not necessarily reflect the views of the United Nations.

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poly-substance users have shown altered emotional pattern, characterized by heightened response to negative stimuli and blunted response to positive stimuli (de Arcos et al., 2008).

Accordingly, brain-imaging studies have also documented the neural responses to drug or drug-related cues in addicts (e.g., Garavan et al., 2000; George et al., 2001). In particular, Wang et al. (2010) utilized functional magnetic resonance imaging to examine brain responses in heroin addicts revealing a complex pattern of altered processing of non-drug related affective stimuli and showing both heightened and blunted neural responses to emotions in several areas of the brain and for different stimulus valence.

Chronic emotional impairment has been linked to adverse childhood experience with consequences related to depression, anxiety and risky behaviours (Klein et al., 2007; Krause et al., 2003). In fact, persistent changes in the limbic circuitry, which is associated with emotional response and arousal, seem to be produced during early neurodevelopment by stressors such as childhood trauma (McCrory et al., 2011).

Findings from a recent study (Grant et al., 2011) provide support for this by showing that potentiated amygdala response to sad stimuli observed among unipolar depressed patients may be driven primarily by sensitization of the amygdala, secondary to persistent exposure to elevated glucocorticoids following early life adversity. In fact, acute stress is associated with subsequent amygdala hypervigilance to emotional stimuli (van Marle et al., 2009). In line with these findings of persistent vigilance, enhanced left amygdala activation during the processing of negative emotional faces was observed in youths who experienced severe emotional and physical neglect in foster care or orphanages (Maheu et al., 2010) and in young adults reporting high childhood family stress (Taylor et al., 2006).

The disturbance of emotion-processing among addicted individuals could correspond to a dysregulation of neuro-physiological reactions. For example, the altered emotional response seems to be associated in heroin-abstinent individuals with a dysfunction of the hypothalamus-pituitary-adrenal (HPA axis), characterized by elevated cortisol and adrenocorticotropic hormone (ACTH) basal levels and a consequent lack of response to unpleasant stimuli (Gerra et al., 2003). Also, HPA axis dysregulation has been repeatedly hypothesized to affect the relationship between childhood traumatic experiences, stressful stimuli, emotional changes and substance abuse vulnerability (Gerra et al., 2008; Heim et al., 2002; Schäfer et al., 2010; Shea et al., 2005). Adverse family relationships in childhood, for example, appear associated to significantly reduced salivary cortisol across a behavioural task in adulthood (Luecken et al., 2009). In particular, childhood parental divorce was found associated with attenuated cortisol in young adulthood (Kraft and Luecken, 2009), which may contribute to the inability to cope with emotional stress.

However, little is known about the influence of childhood adverse events reported retrospectively by addicted patients on their emotional response to different stimulus valence. Therefore, in the present study we investigate the responses to neutral and negative stimuli in human laboratory study, and the related HPA reactions to emotional arousal, among abstinent heroin users, in relationship to their perception of childhood neglect experience. Moreover, considering the relevance that has been attributed to childhood trauma for later drug dependence severity, with significant emotional impairment, insecurity in social contacts and phobic fear (Schnieders et al., 2006), we also explored whether or not the severity of addiction was correlated to the emotional responses to neutral and unpleasant stimuli, the history of neglect and the HPA axis hormone reactivity.

We hypothesized that: 1) the greatest HPA and emotional dysregulation to neutral and unpleasant stimuli will be evident in the heroin addicts compared with controls; 2) in abstinent heroin abusers, HPA axis and emotional response to neutral and unpleasant stimuli will be associated with a significant severity of addiction and high levels of childhood neglect perception.

Thirty abstinent heroin addicts, in comparison with 30 control healthy subjects (never exposed to drugs) were investigated and submitted to a test about their retrospective perception of childhood neglect and to both psychosocial scale and hormonal measures in response to neutral and unpleasant stimuli in human lab (Lang slides).

2. Materials and methods

2.1. Subjects

Thirty (30) male heroin-dependent subjects, aged 22–35 years (M ± SD = 29 ± 6 years), with a history of heroin dependence of 3–7 years (M ± SD 5 ± 2.2 years), were included in the study, after written informed consent. They were not paid for their participation and accepted to enter the study as volunteers. They had been using heroin two or three times a day (active principle 5%–10%) for at least 3 years without any abstinence periods. Heroin dependence was diagnosed following Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) criteria; all heroin dependent subjects had used cannabis regularly before becoming heroin addicts. Cannabis use did not continue together with heroin. At the time of the study, the subjects were heroin addicts and not multiple drug-abusers.

Previous continuous consumption of other drugs of abuse and psychotropic agents or excessive alcohol intake was excluded.

The subjects contacted the Addiction Treatment Centres of Parma (Italy) in 2009 for a problematic clinical condition related to drug use.

The participants were the first 30 residential treatment patients (inpatients: therapeutic community program) who accepted to take part in the study and completed the procedure, in chronological order, in order to be submitted to the experiment after 3 months of abstinence from heroin and any other drug or alcohol.

To obtain the sample of 30 patients, 35 subjects were initially recruited. Five (5) subjects were later excluded because they were not abstinent for 3 months or did not complete the experimental procedure.

All of the subjects accepted also to attend a psychosocial rehabilitation program, as inpatients: the inpatient treatment included group therapy, cognitive-behavioural treatment and educational interventions. Baseline and twice-a-week analysis for urine metabolites of the main substances of abuse (morphine, methadone, cocaine, cannabis, amphetamine-derivatives, benzodiazepines, barbiturate and ethanol) excluded their consumption of drugs for 3 months and confirmed the use of heroin immediately before seeking treatment.

Exclusion criteria included poly-drug use, severe chronic liver or renal diseases or other chronic physical disorders, recent weight loss or obesity, endocrinopathy, immunopathy and, in particular, HIV disease. In compliance with the rules of the program, the subjects were smoking not more than 3–5 cigarettes per day and drinking not more than 2 cups of coffee daily, during the week before the study. They abstained from smoking or drinking caffeinated beverages for the 12 h before our biochemical investigation.

Thirty (30) male healthy volunteers, recruited from the hospital staff and among university students, and matched for age 20–34 years (M ± SD = 28 ± 7.4 years), were used as controls. Exclusion criteria from the study were the same as those used for the patients. Volunteers

Table 1
Demographic and clinical characteristics of sample (n = 60).

	Abstinent heroin addicts	Healthy controls	p-Val
Age years: mean ± SE	29 ± 6	28 ± 7.4	NS
Years of dependence	5 ± 2.2	–	NS
Living in the family rate (not alone) %	74	78	NS
Married %	46	52	NS
Employment rate %	59	88*	<0.01
Educational years: mean ± SE	9.5 ± 0.2	10.8 ± 0.4	NS
Caucasian race %	100	100	NS