

**New-onset Intermittent Explosive Disorder (IED); metabolic and clinical correlates:  
Case report**

Spina Giuseppina Selene<sup>1</sup>, Maria Rosaria Anna Muscatello<sup>1</sup>, Domenica Campolo<sup>2</sup>, Zanotti Mariachiara<sup>1</sup>

<sup>1</sup>Department of Biomedical and Dental Sciences and Morphofunctional Imaging, University of Messina, Italy

<sup>2</sup> Psychiatric Unit, Policlinico “G. Martino”, Messina

Email Corresponding author: [giosenia@hotmail.it](mailto:giosenia@hotmail.it)

**Abstract**

This paper presents the correlation between Intermittent Explosive Disorder (IED), listed in the domain of Disruptive, Impulse-Control and Conduct Disorders in the Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM 5), and metabolic alterations. A 64-years-old man with no previous history of major psychiatric disorders, presenting an onset of IED almost concomitant with the diagnosis of diabetes mellitus and dyslipidemia, is assessed upon a clinical and neuropsychological evaluation. Authors emphasize the influence of metabolic alterations and

liver disease in the manifestation of impulsive aggression and violent behaviour, suggesting a multidisciplinary approach of those patients who present IED and concomitant metabolic alterations.

**Key words:** Intermittent Explosive Disorder, Diabetes Mellitus, Metabolic alterations.

## Introduction

Intermittent explosive disorder (IED), also known as disruptive mood regulation disorder, is characterized by the episodic presence of recurrent acts of affective aggression and failure to resist aggressive impulses that result in assaultive acts towards persons and/or objects (Coccaro, 2012). In the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition – DSM 5 (APA, 2013), IED is listed in the domain of the Disruptive, Impulse-Control, and Conduct Disorders, along with Oppositional Defiant Disorder and Conduct Disorder. With its lifetime prevalence of 4-6%, IED was once thought to be fairly rare, although it is widely recognized that the disorder may be more frequent than thought (Kessler et al., 2006). The first symptoms and signs of the disorder usually appear in adolescence; although individuals with IED consider their behaviour distressing and problematic, reporting significant psychosocial impairment, poor quality of life, and marital and legal problems, often they remain undiagnosed and untreated until late life.

From a psychopathological point of view, IED is a categorical expression of impulsive aggression; aggressive outbursts, involving verbal and/or physical assault, and destructive and non-destructive property assault, have a rapid onset with little or no prodromal period, and are grossly disproportionate to any provocation or psychosocial stressor. Aggressive episodes are associated with subjective distress, significant impairment in social and occupational functioning, relational difficulties, and often with legal or financial problems. Compared with healthy controls, IED patients demonstrate a number of psychological and cognitive features, such as

affective lability and intensity, the tendency to hostile attribution bias and to display greater negative emotional responding to socially ambiguous stimuli, and a greater use of immature defense mechanisms, mainly projection, dissociation, and acting out (McCloskey et al., 2008). Although IED usually appears at young age, in mid-adolescence.

Beyond a substantial genetic component, and a number of neurobiological findings providing evidence of serotonergic abnormalities in limbic areas (the anterior cingulate) and in the orbitofrontal cortex, IED has been associated with diabetes, hypertension, and metabolic syndrome or insulin resistance syndrome (Coccaro et al., 2014). Moreover, impulsive behaviours have been related with hypertriglyceridaemia (Adams et al., 2015), hyperuricemia (Sutin et al., 2014), obesity, and low high-density lipoprotein-cholesterol (HDL-C) (Loas et al., 2016).

#### Case description

P.B. is a 64-years-old man, married, with higher education (degree) and no previous history of major psychiatric disorders. His medical records included an acute ischaemic heart disease treated with percutaneous transluminal coronary angioplasty, diabetes mellitus, an unspecified liver disease still undergoing diagnostic evaluation, and brain chronic microvascular ischaemic disease. He attended our Outpatient Psychiatric Unit because of the occurrence of violent behaviour that caused him legal problems. Within the last few years he had become excessively impulsive, irritable, dysphoric, verbally aggressive and nervous; such personality changes and his symptoms of hostility and aggressiveness had recently become more severe, causing him criminal charges for anger outbursts and aggression directed toward other persons. His premorbid personality was described as extraverted, optimistic, sociable, although impulsive and

dysphoric traits were still evident, with several episodes of loss of control on behaviour. No history of alcohol and/or substances abuse was recorded. The psychiatric interview did not evidence the actual presence of psychotic symptoms (delusions and/or hallucinations); he presented labile mood, poor impulse control, and poor insight into his behavioural and personality changes. The results of routine laboratory tests showed thrombocytopenia, hypertriglyceridemia, hypercholesterolemia, and increase of gamma glutamyl transferase (GGT), aspartate aminotransferase (AST), and alanine aminotransferase (ALT).

MRI examination evidenced hyper intense foci in the periventricular and in the right frontal subcortical white matter, probably of gliotic nature, and a small asymmetry of the lateral ventricles. Doppler ultrasound of carotid arteries showed plaques causing a stenosis of about 35% of the right side of the carotid bifurcation, and up to 20 – 25% of the left one. Neurological examination evidenced psychomotor retardation; sensory examination was intact to temperature, pain, proprioception and vibration, and there were normal tone and strength on motor examination. No tremors, adventitious movements, and dystonia were found. Finally, the patient underwent a neuropsychological and psychodiagnostic assessment including the following instruments:

- Short Neuropsychological Examination - Esame Neuropsicologico Breve - ENB - (Mondini et al., 2003), a battery exploring several cognitive domains (attention, executive functions, and perceptive and praxis abilities) and including thirteen tests: Token Test, Trial Making Test, Digit Span, Logical Story, Interference Memory, Cognitive Estimation, Abstract Verbal Reasoning, Phonemic Fluency Test, Clock Drawing test, Overlapping Pictures Test, Spontaneous Drawing, Copy Drawing, Ideative and Ideomotor Praxis Test.
- Profile of Mood States – POMS – (Mc Nair, 1971), a list of 65 adjectives which measures psychological distress in healthy, physically ill, and psychiatric populations. Six subscales are scored:

Tension/Anxiety, Anger/Hostility, Vigor/Activity, Fatigue/Inertia, Depression/Dejection, and Confusion/Bewilderment.

- Barratt Impulsiveness Scale – BIS-11 (Barratt, 2000) a self-report measure of impulsivity.
- State Trait Anxiety Inventory – STAI (Spielberger et al., 1983), a 40 items self-report questionnaire assessing anxiety as a transient state and as a trait, conceptualized as a relatively enduring disposition to feel stress, worry, and discomfort.

Neuropsychological examination revealed that cognitive functions were globally preserved, since no deficits in tests dependent upon the frontal lobe (attention, verbal, motor and graphomotor abilities, executive functioning, and conceptual thinking) were found; only interference memory resulted mildly impaired.

Table 1: Neuropsychological examination.

<b>Test</b>	<b>Score</b>	<b>Cut-off</b>	<b>Result</b>
Digit Span	6/8	5	Normal
Instant Logical Story	18/28	6	Normal
Delayed Logical Story	21/28	9	Normal
Interference Memory – 10 sec	3/9	3	Within limits
Interference Memory – 30 sec	1/9	3	Below the limits
Trail Making Test – A	46	68	Normal
Trail Making Test – B	89	200	Normal
Token Test	5/5	5	Normal
Phonemic Fluency Test	10	8	Normal

Abstract Verbal Reasoning	5/6	4	Normal
Cognitive Estimation	5/5	4	Normal
Overlapping Pictures Test	32	27	Normal
Copy Drawing	2/2	2	Normal
Spontaneous Drawing	2/2	2	Normal
Clock Drawing Test	10/10	7	Normal
Ideative and Ideomotor Praxis Test	6/6	6	Normal
<b>Overall Rating</b>	<b>73/100</b>	<b>61</b>	<b>Normal</b>

Regarding the POMS, high scores were found at the factors Anger/Hostility (T-score = 86, range = 40 – 60), and Tension/Anxiety (T-score = 71, range = 40 – 60); the scores obtained at the factors Depression/Dejection, Confusion/Bewilderment and Fatigue/Inertia were at the upper normal limit.

Table 2: Poms profile.

<b>POMS</b>	T	D	A	V	S	C
<b>Profile of Mood States</b>	Tension/ Anxiety	Depression/ Dejection	Anger/ Hostility	Vigor/ Activity	Fatigue/ Inertia	Confusion/ Bewilderment
Scores	22	20	34	8	11	16
T – Scores	<b>71</b>	<b>63</b>	<b>86</b>	38	<b>61</b>	<b>67</b>

The self-report evaluation of impulsivity (BIS-11) and anxiety (STAI) resulted within the normal range.

## Discussions

In this clinical case, aggressive outbursts indicative of IED were associated with metabolic alterations, suggesting an organic pathway, considering the significant alterations in blood chemistry evidenced by laboratory examinations. The onset of IED was almost concomitant with the diagnosis of diabetes and dyslipidemia. MRI findings were quite aspecific and the patient's performance at neuropsychological tests was normal, except for the evidence of a suboptimal functioning of the memory resistance to interferent stimuli. The formal integrity of cognitive and executive functions allows us to actually exclude the presence of a degenerative process: both mild cognitive impairment (MCI) and early phase of dementia could be excluded. It is known that some subtypes of IED may be associated with the metabolic syndrome. The "Western diet" (a diet enriched with saturated fat and cholesterol), obesity and insulin-resistance contribute to the onset of affectivity disorders, and interfere with pharmacotherapy (Sonawalla et al., 2002; Shelton and Miller, 2010). Several studies have examined the relationship between lipid profiles and depression, anxiety, impulsivity, suicide, and violence, with low total cholesterol (TC) related to violent and impulsive behaviours in male forensic psychiatric patients (Paavola et al., 2002). A number of reports discussed the above relationships from the viewpoints of decreased serotonergic transmission on impulsive and aggressive behaviours, supporting the hypothesis that reduced cholesterol levels resulted in reduced central serotonin transmission (Huang and Chen, 2005). Contrasting findings have shown an increase of cholesterolemia correlated with depression and anxiety symptoms, and a diet with low intake of  $\Omega$  - 3 polyunsaturated fatty acids (PUFAs), such as Eicosapentaenoic and Docosahexaenoic acids (EPA and DHA), and an elevated  $\Omega$  - 6 :  $\Omega$  - 3 ratios is related to psychiatric manifestations concerning depression, uncontrolled urges (cognitive and motor impulsivity) and hostility in non-psychiatric samples (Conklin S. M. et al., 2006). Also, a relative

deficiency in dietary  $\Omega$  - 3 PUFAs has been implicated in major depressive disorder (Hibbeln and Salem, 1995; Freeman, 2000; Logan, 2003; Peet and Stokes, 2005), attention deficit hyperactivity disorder (Richardson and Puri, 2002), and aggressive behaviour (Hallahan and Garland, 2004).

Mice subjected to a high-cholesterol diet to induce non-alcoholic fatty liver disease (NAFLD) display impulsivity and increased depressive- and anxiety –like behaviours, in response to a Toll like receptor factor 4 (Tlr-4) upregulation in the brain (Strekalova et al., 2014).

Also hepatic illnesses have been associated with impulsivity; in HCV patients poor impulse control has been found, and it has been associated with further psychopathological alterations and high rates of psychiatric comorbidity, with a higher prevalence of depressive and bipolar disorders, anxiety, fatigue, psychotic symptoms, alcoholism and drug abuse (Bruno Copio Fabregas et al, 2014). The patient of this case report is not HCV positive, but shows high levels of transaminases and gamma glutaryl transferase, suggesting a liver disease (actually in course of detailed diagnostic study).

## Conclusions

The correlation between metabolic alterations and IED is supported in clinical studies, especially the relationship between hypercholesterolemia and impulsivity.

Beyond psychopharmacological treatment, an appropriated caloric restriction dietary regime (low-fat diet) might provide a potentially useful approach for those individuals who present IED, mood swings, and dysphoric symptoms associated with metabolic alterations. Furthermore, there is no evidence in literature of a relationship between hypertriglyceridemia and affective/mood shifts or impulsivity; the present case report might suggest to further



investigate possible relationships among IED onset and metabolic parameters, in order to better understand those patients who present the onset/recrudescence of affective alterations and behavioral problems concomitant with metabolic syndrome. Further studies, well designed and performed on sufficiently powered samples, are needed.

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