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NEUROSCIENZE CLINICHE E SPERIMENTALI

"Suicide prevention: investigating a complex phenomenon"

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"It is the paradox of suicide that the victim,
finding inner death in life,
seeks inner life in dying "
John T. Maltsberger, 1980

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1. Introduction

1.1 Some Epidemiological Data about Suicide

Suicide is a complex phenomenon deeply rooted in human nature that is defined as is the act of intentionally causing one's own death. Psychic pain, psychache, desperation, hopelessness, helplessness, aloneness, bitter sorrow and anger overwhelm those who choose death to life (Shneidman,1985).

Evidence shows that suicide rates are rising all over the world and the World Health Organization launched a warning that there will be a 20% increase of death by 2020 and underlined that every 40 seconds someone dies by suicide and many more people attempt it (WHO, 2014). Suicides resulted in 828,000 global deaths in 2015, an increase from 712,000 deaths in 1990. This makes suicide the 10th leading cause of death worldwide. In Genoa, suicide rates are quite high compared with those of other Italian cities and adolescents are increasingly concerned with this phenomenon (ISTAT, 2014).

Suicidal behaviours in college students have been thoroughly investigated and the WHO Mental Health Survey showed that college students had significantly lower twelve-month prevalence of suicide thoughts and behaviors compared with same age peers not in college, 1.9% and 3,4% respectively (O.R. 0.5; $p<0.01$) (Mortier et al., 2018a). Moreover, the study of the prevalence of suicidal thoughts and behaviors in first-year college students in eight different countries showed that 32.7% of the sample had lifetime prevalence of suicidal ideation, 17.5% of suicide plans, and 4.3% had attempted suicide. Besides, 12-month prevalence of suicidal ideation was 17.2%, suicide plans 8.8%, and suicide attempts 1.0% (Mortier et al., 2018b). Of this

population, approximately one quarter (24%) of participants were classified with suicide risk, though rates differed between females (26.1%) and males (20.4%). Overall, sluggish cognitive tempo was indicated as a significant predictor of increased suicide risk (Becker et al., 2018). Interestingly, U.S. medical student suicide rates were lower than those of the contemporaneous general population although significant gaps exist in the knowledge of medical student suicide rates, risk factors, and targets for intervention (Blacker et al., 2018).

1.2 Methods to attempt suicide

The most commonly used method of suicide varies between countries, and is partly related to the availability of effective means. Common methods of suicide include hanging, pesticide poisoning, and firearms in Europe (WHO, 2014).

1.3 Risk Factors

Completed suicides as well as suicide attempts are complex phenomena determined by the interplay of different factors which interact in a complex network. Here, as follows, we review some of the major risks factors related to suicidality that may be helpful to better understand our study.

Previous Suicide Attempts

One of the most relevant risk factors for the development of suicidal ideation is the presence of a positive history of previous suicide attempts. Overall, 40-55% of patients who attempted suicide had a history of prior suicide attempts (Rudd, 2006; Scoliers et al., 2009). A suicide attempt is associated with the risk of both additional suicide attempts (Owen et al., 2002) and completed suicides (Scoliers et al., 2009). Those who

commit multiple suicide attempts –defined as "multiple attempters" - may be considered a cohort of patients who are at high suicide risk. The main characteristics of this group are: (1) female gender, (2) young age, (3) difficult socio-economic situation, (4) severe psychiatric disorders and comorbidity with other mental conditions (Groholt et al., 2009; Brezo et al., 2008; Courtet & Thuile, 2010; Osvath et al., 2003). Furthermore, this specific population has a high presence of suicide attempts or completed suicides in next of kin and this represents an independent risk factor for suicidal behaviors (Monin et al., 2012). Females are at higher risk to be hospitalized for repeated suicide attempts compared to males: this has been estimated to range approximately from1,2 (Chien et al., 2013) to 2,7 (Da Silva Cais et al., 2009) compared with the risk of male controls. However, a British study on multiple attempters reported no gender differences (Bennewith et al., 2002) while an Irish study showed suicide attempts to be higher in males, maybe linked with a widespread alcohol abuse in the local population (Corcoran et al., 2004).

Among adolescents, common risk factors - apart from a positive history of suicide attempts in the family- substance abuse, history of sexual abuse, chronic medical conditions and psychotic disorders, which were predictive of another suicide attempt within a year from the first attempt occurrence (Vajda et al., 2000), may be considered. The frequence of repeated suicide attempts lowers with age (Chien et al., 2013; Bradvik et al., 2009). Concerning age, male multiple attempters are among aged20-35 years, while women aged 35 - 44 years old (Osvath et al., 2003). However, the majority of studies failed to show a significant age difference between single and multiple suicide attempters (Fullerton-Gleason, 2005). Moreover, males are more likely to repeat suicide attempts shortly after the previous one (Suominen et al., 2009). Particularly, 16% of the subjects reattempt suicide within a year (Owens et al., 2002). This percentage raises to

30% within the second year (Bille- Brahe et al., 2002) and remains unvaried until the fourth and fifth years from the first attempt (Kapur et al., 2006).

Major depressive disorder, anxiety disorder, and substance abuse are among the most commonly encountered conditions in multiple suicide attempters (Monin et al., 2012). Moreover, major depressive disorder and substance abuse are notoriously correlated with suicide attempts and suicidal ideation (Bolton et al., 2010), while there are conflicting evidence about anxiety disorders. Some studies have not found any difference regarding anxiety disorders between suicide attempters and non- attempters (Goldston et al., 1998) while other studies seem to suggest significant correlations between panic attacks, post-traumatic stress disorder (PTSD), suicide attempts (Bolton et al., 2010; Krysinska et al., 2010), and repeated suicide attempts (Monin et al., 2012; Lopez- Castroman et al., 2011). Furthermore, multiple suicide attempters seem to have more often a history of clinically significant psychiatric disorders when compared with single suicide attempters. Major depressive disorders, anxiety disorders, substance abuse, and personality disorders, especially borderline personality disorders, were the most common conditions among multiple suicide attempters (Da Silva Cais et al., 2009; Scoliers et al., 2009; Giegling et al., 2009; Osvath et al., 2003). Studies that investigated differences in term of gender in multiple attempters showed that anxiety disorders, major depressive disorders, and PTSD were more more common among females, whereas males had a more severe substance abuse, mainly alcohol, and were more often unemployed (Monin et al., 2012; Osvath et al., 2003). Concerning psychotic disorders there is no concluding evidence: some studies found that psychosis should be considered a risk factor among males multiple attempters (Osvath et al., 2003), while other studies reported hallucinations as significant risk factors among females multiple attempters (Kapur et al., 2006). These data suggested the necessity of organizing preventive strategies for multiple attempters based on gender (Monin et al., 2012).

Psychiatric Disorders

It has been estimated that at least 90% of completed suicides suffer from mental illness; furthermore, a diagnosis of any mental disorder enhances the risk of suicide by approximately 47-74% (Cavangh et al., 2003). Mood disorders, substance abuse, and substance-related disorders andpersonality disorders are among the most dangerous conditions for subsequent suicidal behaviors (Suominen et al., 1996).

Major depressive disorder is among the major risk factor for both completed and attempted suicides (Hawton &Van Heeringen, 2009). Evidence shows that depressed subjects were 20 times more likely to be at risk of suicidal behavior compared to healthy controls (Osby et al., 2001) and that 15% of depressed subjects have attempted suicide at least once in their life considering the non-clinical population (Malone et al., 1995) (in the clinically depressed subjects suicide attempts occurred in approximately 40% of the sample (Malone et al., 1995). Factors positively associated with a higher suicidal risk among depressed patients are: female gender (Osby et al., 2001), severe depressive symptoms (Roy, 2003), personal and family history of suicide attempts or completed suicides (Oquendo et al., 2007), comorbidity with anxiety disorders, personality disorders (Bolton et al.,2008), substance and alcohol abuse (Classen et al., 2007). Tobacco has been recognized to be a relevant risk factor for suicide in the depressed population due to the fact that depressed subjects who regularly smoke tobacco reported higher levels of impulsiveness and aggressiveness compared to depressed subjects who did not (Classen et al., 2007; Mann & Currier, 2010).

In subjects with bipolar disorder, a higher risk of suicide has been associated with rapid cycling, mixed states, mania with marked disphoric characteristics, and agitated depression (Wassermann et al., 2012; Rihmer, 2007), while suicidal behaviors seem more rare in mania with predominant euphoria (Rihmer, 2007). Moreover, an early onset and higher number of episodes resulted associated with higher risk for suicide,

poor outcome, and impaired social functioning. In particular, the risk for suicidal behaviors was higher in the first years after the diagnosis of bipolar disorder as well as in the presence of a comorbidity with alcohol and other substances abuse (Rihmer, 2007).

The exact relationship between suicidal behaviors and anxiety disorders is not yet clear. Evidence shows a lifetime association between anxiety disorders, suicidal ideation, and suicide attempts among adolescents and young adults (Carter et al., 2003; Hill et al., 2011). However, some studies showed that this relationship among adolescents did not persist after controlling for major depression (Foley et al.,2006; Thompson et al., 2005). Conversely, anxiety traits such as chronic preoccupations and alarm, were significantly correlated with suicidal ideation and suicide attempts among young adults independently from the presence of major depression (Goldston et al., 2006). Among adults, PTSD and panic attacks were significantly associated with a higher risk of single (Bolton et al., 2008) and repeated suicide attempts (Monnin, 2012).

Alcohol and other substance abuse are among the major risk factors for suicidal ideation and behaviors both when present as single disorder and/or in comorbidity (Bolton et al., 2008; Krysinska et al., 2010). Males affected by substance abuse seem to be more likely to engage in suicidal behavior than females. Alcohol abuse may be associated with suicidal ideation and attempts in different ways, i.e. acute intoxication has been associated with sedation and thus it could be often used as self-medication by suicidal patients who were likely to seek relief from their sufferings (Wasserman et al., 2012). Furthermore, chronic alcohol abuse may facilitate brain deterioration leading to increased aggressiveness, impulsiveness, depression, and hopelessness (Wasserman et al., 2012). Hopelessness, a negative perspective regarding the future and described as playing a fundamental role in depression, may be also considered a key element throughout the suicidal process. Depression, and in particular hopelessness, may be

considered as strong predictors of suicidal behavior (Pompili et al., 2011b, 2013). More than 50% of suicide attempts in patients with chronic alcohol abuse are carried out during acute intoxication and are usually less severe compared to those carried out by depressed non abusers subjects. Suicidal ideation and suicidal planning could be reduced by the increase of impulsiveness related to the effects of alcohol (Suominen et al., 1996). Among substance abusers, opioid dependent abusers seem to have the higher risk for suicidal ideation and behaviors compared to stimulants and hallucinogens abusers (Maloney et al., 2007). In particular, a case-control study showed that 66% of opioid dependent abusers had ongoing suicidal ideation whereas among stimulant abusers, suicidal ideation was present in 55% of these subjects. Among opiate abusers, 31% had attempted suicide at least once in life (Maloney et al., 2007) and poli-abusers had an even higher risk for suicidal behaviors (Roy, 2002).

For what concerns eating disorders, a large study including a follow-up period of eight years showed that 15% of the subjects attempted suicide at least once during the study time frame. Of these subjects, 22% had a diagnosis of anorexia nervosa and 11% bulimia nervosa (Franko et al., 2004). Evidence showed that suicidal ideation and suicide attempts among subjects diagnosed with eating disorders were significantly associated with comorbid major depression, alcohol abuse, social phobia, and obsessive-compulsive disorder (Wasserman et al., 2012).

Schizophrenia patients had a significantly higher risk for suicidal ideation and suicide attempts compared to the general population. Suicidal thoughts and suicidal ideation had a particular pervasiveness in schizophrenia patients and evidence showed their presence in 30-50% of these patients (Meltzer, 2001). The rate "suicide attempts versus completed suicides" is significantly lower in this population and has been estimated to be approximately 5-10 suicide attempts for every completed suicide. This is presumably due to the use of more lethal methods to attempt suicide compared to other psychiatric

populations (Barak et al., 2008). It has been estimated that 20-50% of schizophrenia patients attempt suicide at least once in their life (Meltzer, 2001) and 15% of patients also attempted suicide once before the first contact with mental health services (Addington et al., 2004). Moreover, a further 15% of schizophrenia suicide attempts occurred within the first five years after the first contact with mental health services (Addington et al., 2004). A Finnish study compared a large sample of schizophrenia patients hospitalized for a severe suicide attempts with a large group of patients hospitalized for a serious suicide attempts but without a psychiatric diagnosis. Schizophrenia patients had a significantly higher risk to reattempt suicide (58% of the group) and complete suicide (78%) compared to the other group without psychiatric diagnosis throughout the course of 3,6 follow-up period (Haukka et al., 2008). Being young, being male , having low social support and scarce treatment compliance, substance abuse, fear of mental disintegration, having multiple prior depressive episodes, and abundant positive symptoms were reported as factors predisposing to suicidality (Kelly et al., 2004; Hawton et al., 2005). Though a large body of literature attempted to differentiate suicidal schizophrenia patients from schizophrenics who were not at risk for suicide, evidence suggested that this is a still open debated question (Hawton et al., 2005). Though the communication of suicidal ideation and intent in schizophrenia is not simple due to its formal characteristics of thoughts and contents, evidence showed that in a sample of schizophrenia patients this comunication resulted not significantly different compared to a group of non-psychotic patients (Heila & Lonnqvist, 2002). Subjects with first episodes psychosis (FEP) should be carefully evaluated for the presence of suicidal thoughts and suicidal ideation as there are studies showing that 21,6% of patients who attempted suicide and 4,3% who completed suicide carried out the act within the first seven years after the onset of psychosis (Robison et al., 2010). Among subjects who were more likely to attempt suicide early after the onset,

being female and single, as well as having higher educational level have been suggested as specific risk factors for suicide (Levine et al., 2010). Furthermore, affective symptoms during FEP should be carefully evaluated as significant predictors of suicide (Robison et al., 2010).

Recently, the scientific community focused its attention on suicidality in adolescents diagnosed with pervasive developmental disorders (PDD). A Japanese group found that in a sample of 94 adolescents hospitalized for a suicide attempt, 12,4% had a diagnosis of PDD and showed a significantly lower presence of comorbid affective and anxiety disorders compared with adolescents without PDD formulated through the Autism – Spectrum Quotient Japanese version (AQ-J) (Mikami et al., 2009). Among pervasive developmental disorders, the most common Diagnostic and Statistical Manual (DSM) Fourth Edition Text Revision (TR) diagnosis among suicidal adolescents was Asperger Syndrome and PDD not otherwise specified (NOS) (Mikami et al., 2009). Overall, subjects diagnosed with Asperger Syndrome resulted more likely to engage in suicidal behaviors due to the better relational and social skills of this group compared with the other PDD. Asperger subjects may be more aware of their impairments and this would foster feelings of loneliness, isolation, and rejection despite the rigidity of thoughts. Evidence showed that Asperger subjects usually choose highly lethal methods to attempt suicide (Gillberg, 2002).

Personality Disorders have been often reported as comorbid conditions with DSM-IV TR axis I disorders among suicidal patients. Overall, 44% of suicidal patients reported an Axis I and Axis II comorbidity (Hawton et al., 2003) and 55-70% of subjects who attempted suicide at least once received one or more personality disorder (Schneider et al., 2008). Borderline personality disorder has been identified to be at higher risk to develop suicidality and evidence showed that 75% of those with borderline personality disorder attempted suicide at least once in life (Black et al., 2004). A history of

childhood abuse – physical, sexual or both – and a diagnosis of PTSD significantly enhanced the risk of suicidal behavior among borderline subjects (Black et al., 2004). The high risk of suicidal behaviors in this group could be conceptualized in the light of the high impulsiveness and emotional dysregulation associated with this condition (Giegling et al., 2009). Antisocial and avoidant personality disorders have been significantly associated with a higher risk to develop suicidal ideation, though to a lesser extent if compared with borderline personality disorder (Duberstein et al., 2000). The study of suicidal behavior in subjects with personality disorders showed a higher frequency of negative life-events in the month before the suicide attempt; this could facilitate the gesture in the light of the scarce coping strategies, high aggressiveness, impulsiveness, hostility, anxiety, and primitive defense mechanisms of this population (Stanley et al., 2009).

Personality traits have been investigated in relationship with suicidality and evidence showed that anger, impulsiveness, and aggressiveness were among the most related dimensions to suicidality. Depressed women with suicidal ideation, history of violent or non- violent suicide attempts had significantly higher levels of aggressiveness and impulsiveness compared to non-suicidal depressed women (Giegling et al., 2009). Some authors (Mann et al., 2008; Oquendo et al., 2004) identified severe aggressiveness and depression as predictors of the development of suicidality in both males and females. Moreover, anger- related personality traits were often related with impulsiveness and aggressiveness in suicidal patients (Kirkcaldy et al., 2006) and impulsiveness, aggressiveness, and pessimism have been identified to significantly increase suicide risk after depressive episodes (Oquendo et al., 2004).

Studies concerning affective temperaments and personality traits showed that suicidal patients often had high levels of "novelty seeking" and "harm avoidance" together with lower "self-directedness" and "cooperativeness" when compared to non-suicidal

patients (Giegling et al., 2009). A Canadian group reported an association between impulsive and aggressive personality traits that could form an impulsive-aggressive lifetime dimension significantly predisposing subjects to develop suicidality (McGirr & Turecki, 2007). However, when investigating the effects of impulsiveness on suicidal ideation, there are studies showing that younger subjects without psychiatric conditions were more likely to have higher impulsiveness and proceed from suicide ideation to suicide attempt without planning the gesture. Conversely, the presence of mental disorders and older age were more frequently associated with the progression from suicidal ideation to suicide attempts through suicidal plans (Levinson et al., 2007). Furthermore, the risk of progression from suicidal ideation to suicide attempts is higher in the first year after the onset of suicide ideation independently of impulsiveness levels (Levinson et al., 2007). The role of anger in the progression from suicide ideation to attempts through suicide plans is not so clear-cut. While certain studies showed that high levels of anger increased impulsiveness concerning the attempt (Jollant et al., 2005), other studies failed to confirm this result, in particular concerning the role of anger in the process of decision-making and suicidal planning (Martinotti et al., 2008).

Other Risk Factors

The exposure to a wide range of adverse life events has been significantly associated with an increased vulnerability to develop suicidal ideation and suicidal behaviors (Pompili et al., 2011a). In particular:

- Stressful life events during childhood, e.g. parents' separation and divorce; important family discord (Fergusson et al., 2000);
- History of childhood physical and/or sexual abuse (Molnar et al., 2001);
- Childhood neglect (Johnson et al., 2002);

- Low social support (Pompili et al., 2011a);

- Losses (e.g. grieves) and interpersonal conflicts that have been identified as important triggers for suicidal behaviors (Pompili et al., 2011a)

Studies that investigated the most important triggers for suicidal behaviors showed a significant interplay between childhood and adolescent stressful life events occurring in the months before the development of suicidality.

Stressful life events occurring in the six months before suicide attempts were more likely to be present among the subjects who attempt suicide for the first time compared to repeaters (88.8% vs. 78.7%) (Pompili et al., 2011a). Subjects who repeatedly developed suicidal ideation and carried out repeated suicide attempts were more likely to have a history of early stressful life events and trauma (Pompili et al., 2011a), however there are studies that failed to confirm these results (Chandrasekaran et al., 2008). Both a single and cumulative lifetime effect has been hypothesized for the role of stressful life events in suicidal behavior. Pompili and colleagues (2011a) suggested that risk factors can either predispose to attempt suicide at an earlier age and, as a kindling phenomenon, determine a "suicide career" or, alternatively, an accumulation of stressors may produce a "last straw" effect. The kindling effect is used to describe diseases where each episode of the illness later enhances more frequent and severe episodes (Johnson et al., 2002). Similarly, risk factors may increase their strength each time the suicidal individual makes an attempt, and certain risk factors may come into play at a given time, even long after the suicide career has been developed. Conversely, in the case of the "last straw" effect, an accumulation of stressors is the central characteristic in determining suicide attempts (Pompili et al., 2011a).

Studies that investigated the role of early sexual abuse showed that it significantly increased the risk of suicidality, PTSD, major depressive disorder, impulsiveness, aggressiveness, and hostility not only in the abused victim but also in his offspring (Brodsky et al., 2008).

Sexual abuse appears to be more tightly related to suicidality than physical abuse (Anderson et al., 2002); furthermore, when comparing the offspring of physically abused victims and sexual abused victims, the offspring of the latter were at higher risk of suicidality and had higher impulsiveness, though presenting lower aggressiveness (Molnar et al., 2001). Sexual and physically victims may be also considered at higher risk of becoming suicidal (Anderson et al., 2002).

Finally, a strong relationship between psychiatric disorders, medical conditions such as cancer, diabetes mellitus, stroke, dementia, chronic headaches, multiple sclerosis, and suicidal behavior has been reported. Specifically, a strong association has been reported between primary headaches, psychiatric disorders, and suicidal behavior (Pompili et al., 2010); higher suicidal rates have been suggested in patients with multiple sclerosis compared with the general population (Pompili et al., 2012a); and stroke has been documented to confer a substantial risk for suicide (Pompili et al., 2012b).

Importantly, physical illness and chronic pain represent an important risk factor for suicide not only for the related physical pain and altered body function but also for the significant associated psychological distress (Jia et al., 2014).

However, no concluding evidence has been reported and translational research able to bridge research findings with everyday clinical activity largely lacks, thus data helping clinicians to better reach and help those who suffer are still largely missing.

1.4 Gene-Environment Interaction

Environment plays a pivotal role in modulating genes expression in early life stages, thus influencing the epigenome (Mann et al., 2003). Early traumatic events, physical, and sexual abuse may cause permanent alterations in genes expressions that later create a diathesis for psychiatric disorders (Szyf, 2009), suicidality (Evans et al., 2005), a

specific reactivity to stress, impulsivity, and aggressiveness (Mann et al., 2003). Moreover, evidence shows that the prevalence of suicidal ideation and suicide attempts were positively related to both the degree and severity of the abuse (Fergusson et al., 2008; Brezo et al., 2008).

There is clear evidence that the activity of three neurobiological systems has a role in the pathophysiology of suicidal behavior. Specifically, the hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis, dysfunction of the serotonergic (5-HTergic) system, and excessive activity of the noradrenergic system may be significantly implicated. While the first and the last system appear to be involved in the response to stressful events, dysfunction of the serotonergic system has been hypothesized to be trait-dependent and associated with disturbances in the regulation of anxiety, impulsivity, and aggression. It can be postulated that neurobiological dysfunctions mediate the occurrence of suicidal behavior through the disturbed modulation of basic neuropsychological functions located in the prefrontal cortex (PFC) and limbic system (Van Heeringen, 2003). This explains the diathesis of suicidal subjects for major depression (Mann et al., 2010) and impulsive- aggressive traits (Giegling et al., 2009). Methylation is the epigenetic mechanism most relevantly associated with early trauma and was able to cause the silencing of certain genes by preventing the binding of transcription factors to DNA (Labonte & Turecki, 2010). Childhood neglect, early mother separation and physical abuse have been significantly associated with alterations of genes involved in the serotonergic system, such as the serotonin receptor 1A and 1B (5HT1A; 5HT1B); the serotonin transporter (SERT); tryptophan hydroxylase (TPH); serotonin-transporter-linked polymorphic region (5-HTTLPR); monoamine oxidase A (MAO-A) both in humans and rodents (Van Heeringen, 2003). Animal studies showed that even small differences in early maternal care may cause different gene methylation in the hippocampus (Champagne et al., 2008) and that early maternal separation may

cause a decreased functioning of the serotonergic system, that is determined by the presence of the short variant of the promoter of serotonin transporter (5-HTTLPR-S) (Uher & McGuffin, 2007). The 5-HTTLPRS-S in humans is associated with an increased risk for major depression, aggression, and suicide attempts in adulthood (Uher & McGuffin, 2007).

A considerable body of literature shows the relationships between aggression, increased reactivity to stressors, emotional dysregulation, suicidal behavior and two or three tandem repetition variants of MAO-A (2R-MAO-A; 3R-MAO-A) (Bortolato et al., 2013). Childhood abuse and early neglect may mediate the relationship between 2R- and 3R- MAO, aggression (Bortolato et al., 2013) and suicidality in males (Huang et al., 2004). Studies of functional brain imaging showed that the 3R variant was significantly associated with both structural and functional alterations in the orbito-frontal cortex (OFC) and limbic system as well as the hyper-reactivity of the amigdala and hippocampus during tasks of recalling negative life – events (Hung et al., 2012). However, the association between MAO-A variants and suicidality may be considered controversial (Courtet et al., 2005).

Moreover, a considerable inhibition of the BDNF hippocampal production and its receptor tropomyosin receptor kinase B (TrkB) in response to the exposure to acute and chronic stressors has been reported. This may induce impairments in the development of serotonergic system (Sher, 2011) as well as increased risk of suicidal ideation and behaviors in adolescence (Pandey et al., 2008). However, dysfunctions of the serotonergic system seem to be associated only with a diathesis for aggressiveness and suicidality and not with pathological behaviors resulting from a complex interplay between environmental and gene-related factors. The interplay of these variables may induce impairments in emotional regulation and social skills due to altered circuits in

the prefrontal cortex, limbic areas, and raphe nucleus, which determine a diathesis for auto- and hetero-aggressive behaviors under distress (Bortolato et al., 2013).

Studies investigating the involvement of HPA-axis and noradrenergic system in suicidal behaviors reported the existence of a hypersensitivity to stressors among subjects with a positive history of suicide attempts. Childhood abuse and early neglect have been associated with the hyper-reactivity of the HPA-axis with an altered level of neuropeptide Y and corticotropic releasing factor (CRF) (Heim & Nemeroff, 2001) that have been shown to be related with a higher risk of suicidality (Mann, 2003; Pompili, 2010). Subjects with previous suicide attempts had significantly higher values of urinary cortisol in a 24-hour sample compared to subjects who never attempted suicide (Van Heeringen, 2003).

The heritability of suicidal behaviors and suicidality has been estimated to range from 17% to 45%. Studies showed that subjects who had a history of suicide in the family were at a significantly higher risk for suicide compared to subjects without such a history; these results have been confirmed also after being corrected for the presence of psychiatric disorders (Brent et al., 2008). Endophenotypes have been investigated to explain the occurrence of certain behaviors and related genetic variants in suicidal families.

The endophenotypes suggested to be related to suicidal behaviors are:

a. <u>Impulsive and aggressive traits</u>: high levels of impulsivity and aggression are associated with a higher risk to develop suicidality and suicidal behaviors (Oquendo et al., 2004) with highly lethal methods (Placidi et al., 2001). Aggression is a dimensional trait with a heritability of almost 40-47% (Mann et al., 2009). Family studies showed a co segregation of the impulsive/aggressive endophenotype and suicidality (Melhem et al., 2007) and a relationship between impulsivity/aggression with certain genetic variants related to the serotonergic system such as 5-HT2A; 5-

HT1B e MAO-A (Mann et al., 2009). Impulsive traits have been associated with 5-HT2A in subjects with alcohol abuse (Mann et al., 2009).

b. <u>Early onset of depression</u>: studies showed the association between early onset of depression and increased risk for suicidality and suicide attempts (Mann et al., 2009). The Sequenced Treatment Alternatives to Relieve Depression Study (STAR*D) demonstrated a triple risk of suicide attempts among subjects who had the onset of depression before the age of 18 compared to subjects who had this onset in an older age (Zisook et al., 2007). Linkage studies showed an association of alterations in the chromosomal loci 15q, 17p,8p and 6p (Holmans et al., 2007) among subjects who had the first episode before the age of 18 compared to subjects who had the first episode later (Zisook et al., 2007). Linkage studies showed an association between early onset of depression, suicidality, and chromosome variants which were localized in 15q, 17p, 8p, and 6p (Holmans et al., 2007).

c. <u>Neurocognitive functions</u>: evidence showed a considerable number of neurocognitive alterations among suicidal subjects. Subjects who attempted suicide using highly lethal methods had significant deficits in selective attention compared to subjects who attempted suicide using less lethal methods. Furthermore, this may be directly related to impairments in focusing attention and problem-solving tasks (Keilp et al., 2008). Subjects who repeatedly attempt suicide had deficits in focusing attention (Wenzel et al., 2009). These neurocognitive impairments have been shown to have an heritability of 39-50% (Mann et al., 2009) and there is contrasting evidence concerning its relationship with the heritability with depressive disorders (Reppermund et al., 2009; Westheide et al., 2008).

d. <u>Cortisol response to psycho-social stressors</u>: evidence reported that alterations in the HPA-axis were associated to higher suicidality (Mann et al., 2009). Early traumatic events have been proven to be related to a hyperactive response of the HPA axis to psychosocial stressors as well as to particular polymorphisms of mineralocorticoid and glucocorticoid receptors (DeRijk et al., 2008), 5-HTTLPR-S (Gotlib et al., 2008), and the alpha 6 GABA-A receptors (Oquendo et al., 2003).

Moreover, recent studies suggested the existence of additional biological variants that could be considered endophenotypes for suicidal behaviors though it is still uncertain whether these variables fulfill the required criteria to be really considered endophenotypes (Dwivedi et al., 2004; Dwivedi and Pandey, 2011). Further studies are needed to investigate the role of other biological variables, such as brain structure (Dwivedi et al., 2004), and brain metabolism (Dwivedi & Pandey, 2011) in influencing suicidality and identifying further possible endophenotypes.

General Aims of the Study

This project aims to investigate and identify key characteristics of the suicidal mind and brain, which cannot be considered as separated, that could help clinicians in the work and in trying to engage suicidal patients in a therapeutic work.

For instance, our aim is to develop a translational research project, which concerns and bridges three different research areas namely clinical (a) epidemiology and prevention; (b) neurobiology and (c) psychodynamic understandings as their effects are tightly intertwined in leading to suicide.

General Project Design

Three different areas will be investigated using an overall concomitant design encompassing singular designs that best fits the purposes of each of the investigated research areas.

In particular;

- Research area A: Epidemiology and Prevention.

  Cross sectional case- control design

- Research area B: Neurobiology of the brain

  Cross sectional case- control design

- Research area C: Psychodynamic Aspects of Suicide

  Longitudinal, experimental single case study design

The Research Group

The research group with whom I developed the present study is the Suicide Research Group of the Psychiatric Clinic, Dpt. of Neurosciences, Rehabilitation, Ophtalmology, Genetics and Maternal and Infant Health of the University of Genova, School of Medicine.

The Director of the Clinic and Supervisor of the present research project is Prof. Mario Amore. The head of the Suicide Research Group is Prof. Gianluca Serafini. Other members of the Suicide Research Group who were involved in the project are Dr. Andrea Aguglia, Dr. Gabriele Giacomini, Dr. Matilde Caprino and Dr. Claudia Conigliaro.

Study Location

The study took place in the Psychiatric Clinic, Dpt. of Neurosciences, Rehabilitation,

Ophtalmology, Genetics and Maternal and Infant Health of the University of Genova,

School of Medicine from July 2015 to January 2019.

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RESEARCH AREA A

EPIDEMIOLOGY

AND

PREVENTION

An Epidemiological Investigation of Suicide in the Past: from guilt & punishment to disease & care

Introduction

Changing attitudes to suicide are as complex and variable as the very complicated social and cultural systems in which they existed (MacDonald, 1995) since suicide often results from a complex interplay of socioeconomic and cultural factors, which cannot be considered separately.

The current economic crisis has been positively related to suicide rates by several studies (Stuckler et al., 2009; DeVogli et al., 2012), though it is unclear whether economic downturns and unemployment may represent causal factors for suicide (Hawton and Van Heeringen, 2009; Luo et al., 2011; Innamorati et al., 2012; Solano et al., 2012). A number of studies demonstrate that European countries with large fiscal adjustment are notably affected by increasing suicide rates (Breuer, 2015; Karanikolos et al., 2013; Stuckler et al., 2011), nevertheless some country- specific investigations deliver controversial findings. For instance, suicide rates in Greece have been causally affected by the current economic crises (Economou et al., 2012; Kentikelenis et al., 2014; Karanokolos et al., 2013), although contrasting evidence has been reported (Fountoulakis et al., 2013; Polyzos, 2012). Similarly, Neumayer (2004) and Andres (2005) challenged previous findings that unemployment positively affects suicide in a panel of European countries after controlling for country-specific trends. In the same vein, Pompili et al., (2011) suggested that Italian regional suicide rates were directly associated with employment rates and inversely associated with regional household, thus regions with higher economic status would have higher suicide rates. The different results can be partly due to the use of aggregated data for the analysis (Breuer, 2015) or

methodological weaknesses (Andres, 2005), though the relationship between suicide and economic crises still remains an open question involving different sociological and cultural factors.

Society, as is well known, strongly influences man's own sense of self and the way he perceives himself in the world together with his wishes and needs. Murray (1938) in *Explorations in Personality* identified some psychological human basic needs, that if frustrated provoke intense psychic pain involved in suicide. Furthermore, factors such as mental illness may influence the role subjects play in society and how they relate to it together with their working capacity and economic status. These understandings are fostered by a large number of studies suggesting that mental illness plays a pivotal role in mediating the association between unemployment and suicide risk (Lundin et al., 2010) as do public health policies (Stuckler et al., 2009).

However, these understandings, that nowadays appear to be common knowledge, result from the development of an integrated conceptualization of suicide, which gradually began to be considered both as a psychiatric and as a sociological matter of concern. This study examines:

(a)The process that led to the modern conceptualization of suicide together with the changing attitude towards it

(b)The sociological understandings of suicide throughout time

(c)The economic theories developed throughout time to understand the relationship between suicide and economic circles.

Material and Methods

Articles for consideration were retrieved through an extensive literature search for "socioeconomic factors AND suicide"; "economic circles AND suicide"; "history" AND suicide" in MEDLINE, EMBASE and SCHOLAR without timeframe limitations because of the targeted domain. This produced over 500 studies, but only historical papers concerning European countries directly focusing on the subjects were examined for possible inclusion. This led to the inclusion of 42 studies. Additional titles of papers and books were obtained from the bibliographies of these articles, and from a journal-by-journal search for journals in related areas, i.e. history, philosophy, economy and sociology, that we suspected most frequently publish articles in the targeted domain. This strategy was adopted to minimize the possibility of overlooking studies that may not yet have been included in computerized databases. At the end, 51 studies were included.

Suicide and sociological factors: from crime to mental illness

Attitudes towards suicide varied during man's history as suicide, from being one of the most severe crimes against God, Law and Nature, became an extreme act of desperation resulting from the sufferings of mental disorders. Socrates, for example, forbade his disciples from committing suicide except under extreme circumstances and both Plato and Aristoteles considered suicide as an act against an obligation to society. The Stoics, however, thought such a decision as part of human freedom. Furthermore, Ancient Greeks already expressed the concept of self-killing using a single word connected to a specific method to carry out the act such as "*autosfaghe*" meaning "He who is slain by himself", used in Sophocles' Ajax, (Lloyd-Jones H., 1994) and "*autokeires*" meaning "those who kill themselves", used in Euripides's Phoenician Women (Kovacs D., 2002). Furthermore, according to the *Suida,* a scholarly encyclopedia on ancient Greece written at the Court of Byzantium, some verbs meaning "to hang oneself" were used too,

implying "hanging with the aim of being killed by oneself" as in Homer's Odissey (Preti and Miotto, 2005).

In ancient Rome, there were different conceptualizations of self-accomplished death. The Roman law intended suicide as a crime sanctioned with the requisition of the victim's possessions (Farberow, 1975). However, in many Latin Authors, suicide is a very solemn, detached, unemotional act due to relational, philosophical or political matters such as in the case of Cato Uticensis and Thrasea Paetus in Tacitus's writings (Hill, 2004). This kind of suicide that concerns public figures and members of the aristocracy was called "*Romana Mors*". However, these representations of death have been deemed unrepresentative of truth and even defined unreal by some Authors (Alvarez, 1971).

Among the Hebrews, though suicide was infrequently mentioned in the Old Testament, the first formal prohibition may be found when Josephus, in the first century AD, forbade his army from committing suicide following their defeat by the Romans (Churchill, 1994; Crone, 1996). Christianity, in light of the example set by Judas, condemned suicide. Augustine of Hippo formalized this thought in the light of the Sixth Commandment giving no excuses for suicide and, later, Thomas Aquinas considered suicide as against the inclination towards self- preservation, against one's duties towards society and against God's prerogatives as creator of man (Aquinas, T., Lefébure, M., 2006). To address suicide, circumlocutions such as "self-killing" and "self-homicide" which added a judgmental nuance highlighting the link suicide had with homicide, were used. Augustine of Hippo's conceptualization, adopted by the Church till the sixteenth century, classified both suicide and homicide under the heading *crimen homicidi* and suicide victims as well as killers as *homicida* (Augustine of Hippo, 410 AD). Even from a legal perspective suicide was considered no less severe than homicide (Mash, 2010).

The word "suicide" was used for the first time in the seventeenth century (Shneidman, 1985) in Thomas Browne's *Religio Medici.* Until that time "men's underlying moral conceptions were not at the stage of needing a word for so a specific definition, a definition founded, that is, on a particular compound of intention and act" (Murray, 1998 pp. 39-40). The introduction of the word "suicide" is intertwined with the sociological developments of the time, in particular with the change in the conception of the human being, which acquired his own "interiority" apart from the "exteriority" of the world (Taylor, 1989; Strozier, 2002; Martin and Barresi, 2006). Furthermore, the secularization of suicide that took place in England between the middle of the seventeenth century and the beginning of the eighteenth century, led to a gradual decrease in supernatural explanations of phenomena and the development of a more rational and scientific approach, to which the spreading of Enlightenment theories contributed. Overall, suicide became the result of a rational choice mostly related to mental disorders (Rosen, 1971; Brown, 2001; Healy, 2006; Houston, 2010).

Starting from the eleventh century England, when suicide occurred, the act was judged by the local coroner who examined the body and gathered a jury to return a verdict which could be either *felo de se* (i.e., "felon of himself") – thus guilty of self- murder – or *non compos mentis* (i.e., "not sound of mind"), thus innocent of the crime (see Table I).

Felo de se	*Non compos mentis*
"William de Wedmore, vicar of Chryriton hanged himself in his own home in the same village. The verdict was suicide. And Walter de Wedmore and John his brother(s)	"William la Emeyse of his vill, suffering from an acute fever which took away his senses, got up at night, entered the water of Kentford and drowned himself. The jury was

buried the said William without view of the coroner and took his chattels, value 34s so they are to be arrested. Afterwards they came to court and the sheriff let them go. "
(Eyre of Sommerset, 1280)

"A certain Richard, son of Sibill gratis drowned himself in a pit at Marshton St Lawrence. No one is suspected. Judgment felonious suicide. Chattels 6s 2d." (Eyre of Northamptonshire, 1329)"

asked if he did this feloniously and said no, he did this through his illness. The verdict was an accident." (Eyre of Hereford, 1292)

"Thomas, son of Henry Robekyn of Brandon, in a frenzy *(habens frenesium)* cut off his left foot with an axe and then his left hand in the house of the said Henry, his father, in Brandon, and the following night he died from this. The first finder and four neighbours came and are not suspected. The jury, asked if they suspected anyone else of this death say no and say that the said Thomas straight after the deed came to his senses *(reddit ad sensum proprium)* and had the last rites of the church before he died. So the deed was done through the loss of sense and not feloniously. So the judgment is accident ."
(Eyre of Norfolk, 1286)

Table 1. Transcriptions of verdicts from the Eyre rolls, England. The verdict from the Eyre of Sommerset shows the attempts of the relatives to conceal the suicide in order to avoid the forfeiture. The verdict from the Eyre of Hereford shows how the effects of physical illnesses were considered responsible for mental alterations along with mental illnesses. (Adapted from Seabourne and Seabourne, 2001)

The latter verdict meant that the penalties to which the guilty deceased party and his family were condemned did not apply. In England, these penalties implied the forfeit of the deceased's goods to the crown or landlord and a profane burial in a crossroad accompanied by a macabre ceremony on the corpse (Fleming, 1773). This could drive the heirs to pauperism and therefore they, together with parishes, often concealed the real nature of the death or invented stories in order to allow the verdict of "non compos

mentis" (MacDonald and Murphy,1990; Barbagli, 2009; Marsh, 2010). The resistance to forfeiture proceeded more rapidly than the secularization of suicide verdicts, and the records of the Court of King's Bench report a drop in the forfeited goods of suicide victims at the end of the seventeenth century. In the 1660s, 36% of suicide victims had their goods forfeited whereas fifty years later, between 1710 and 1720, the percentage dropped to a mere 7.7 % (MacDonald and Murphy,1990).

At the beginning of the sixteenth century, in order to acquit suicide victims of self-murder and save their goods from forfeiture, English juries began to return "mixed" and "ambiguous" verdicts along with verdicts of *non compos mentis*. *Non compos mentis* verdicts gradually rose from the beginning of the seventeenth to the beginning of the nineteenth century when 90% of suicides were judged as *non compos mentis* (Figure I), thus mirroring an important change in the attitude towards suicide victims that led to the end of what was defined as "the age of severity" (MacDonald and Murphy,1990).
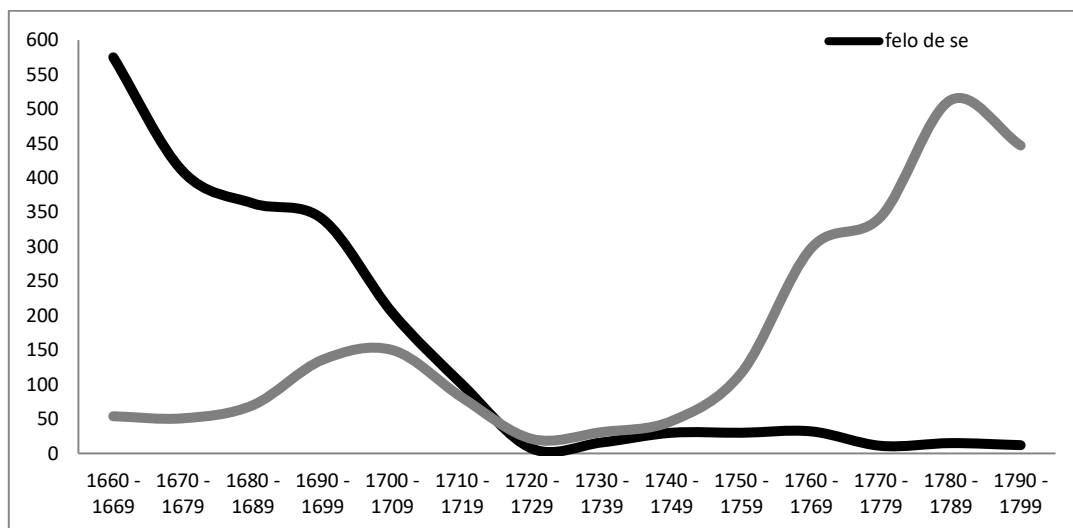

Figure 1. Verdicts of reported suicides in England, 1660-1799. (Source: MacDonald, Murphy, 1990).

However, coexisting different explanations can be found much earlier. Herodotus recorded the case of the Spartan king Cleomenes I whose suicide was considered either as a divine retribution for his acts of impiety or the result of a madness caused by excessive wine drinking (Preti and Miotto, 2005). Moreover, documents dating back to the early sixteenth century reported the beginning of medical and rational approaches to suicide alongside supernatural ones (Table 2a) which, however, was not well accepted by everyone (Table 2b).

Table 2. From crime against society to medical illness: (a) the beginning of the changing attitude already; (b) difficulties in changing the attitude across Europe

In 1502 the Flemish prior Gaspar Ofhuys, who was also the doctor of the monastery, wrote about the suicide of the famous Flemish painter Hugo van der Goes who belonged to his monastery. Ofhuys offered three different understandings of that act: a traditional Christian one which hypothesized a demonic possession of van der Goes; a supernatural one involving the Divine Providence which would have stopped through suicide the ambitiousness of the famous painter-monk and a third one in which the prior hypothesized suicide would have been caused by the ingestion of "melanchonic foods" which would have altered the equilibrium of body humors (Dolev, 1999).	In 1842 the parish of a French village wrote to the bishop of Angers because a young leper woman had committed suicide. The parish believed the woman was mentally insane whereas her family and other people of the village maintained she was sane and asked for a *felo de se* verdict despite his mind (Kselman,1988).

In 1682 a German book-seller after having attempted suicide, asked for help both to the parish and to the doctor (Lind, 2004).	In 1893 a woman in a Russian village drowned herself in a river. Her husband asked for a Christian burial which was allowed despite the strong opposition of the peasants who lived in that village. Some months after her burial some sudden deaths took place in the village which were interpreted by the villagers as a divine punishment for the woman's Christian burial. So her corpse was removed from the graveyard, mutilated and buried in a not-sacred place (Morrisey, 2006).

Eventually, all suicides were considered as resulting from a mental disorder and suicide itself started to be considered as a sign of insanity (Chevalier, 1824; Winslow, 1840). This new understanding paved the way for the medicalization of suicide, which then became something "doctors had the right to guard, treat, control and judge" (Hacking, 1990, p.65). In 1821, Esquirol's *Dictionnaire des sciences médicales* defined suicide as a disease or a symptom of a disease, thus to be medically investigated (Esquirol, 1821). Insanity, which was recognized as the heart of suicide, was investigated according to the attitude of the time through autopsies that aimed to locate physical lesions causing it. However, no evidence was found to support the existence of pathological anatomy related to suicide (ibid.) even though Burrows maintained that this "does not disprove the existence of a morbid condition" (Burrows, 1828, p.416). Akin to Esquirol's formulations, Burrows suggested that emotions, mental and moral faculties could become diseased and different kinds of insanity could arise which later could lead to suicide as the result of a too violent impression upon the brain (Burrows, 1828). Thus, suicide became the result of psychopathology, with the site of pathology either acting

to cause disturbance on the whole organism (e.g. faulty reasoning consequent upon a brain lesion), or causing brain lesions (Esquirol, 1821). Thus, the body became the major source of investigation to understand suicide and suicidal individuals were systematically watched and examined in asylums in order to identify some premonitory signs of their propensity to commit suicide. However, the lack of findings of pathological anatomy thwarted the development of "organic theories" of suicide and Prichard (1835) wrote about the existence of functional disorders of the mind in his *Treatise on Insanity and Other Disorders Affecting the Mind*.

The influence of the Enlightenment on the overall attitude towards suicide and the concept of human life stemmed from an intellectual *querelle* which began at the end of the sixteenth century when philosophers, writers and theologians all over Europe began to wonder about man's right to take his own life, condemning the contemporary Christian conceptualization (Houston, 2010). The first intellectuals who engaged in the *querelle* included Thomas More who defended some forms of suicide in Utopia in 1516, Montaigne in 1580, and John Donne who wrote Biathanathos in 1610. In the eighteenth century Montesquieu, Cesare Beccaria and Voltaire further developed the thesis of man's right to commit suicide since life itself was a man's own property and human beings were unique and had the right to self-realization and to the pursuit of happiness in life. Beccaria and Voltaire in particular were engaged in the struggle to reform the penal system for the decriminalization of suicide. In the wake of the Enlightenment, new intellectual theories were developed including Contractualism, Utilitarianism and neo-epicurean understandings of life. For instance, according to Contractualism, society was a contract stipulated among subjects from which everyone had the right to step back through suicide whenever it became no longer convenient.

In the nineteenth century, as Romanticism spread, the attitude towards suicide changed even further. The rational approach that had characterized the Enlightenment was replaced by a passionate and idealized view of suicide that was celebrated by many famous writers throughout Europe such as Goethe, Schiller and Tolstoj. Under the influence of masterpieces like *The sorrows of young Werther, Anna Karenina* and *The Last Letters of Jacopo Ortis,* a rapid increase in the number of suicides occurred and was defined as a new fashion by Tissot in 1840 in his *De la manie du suicide et de l'ésprit de révolte, de leurs causes et leurs remédes.* However, at the end of the nineteenth century Durkheim (1897) developed his theory of suicide in *Suicide, a study in sociology* according to which society played a pivotal role in determining it. Durkheim suggested that man was modeled by society and social rules inevitably stemmed from the individual ones and then became superior to them through the process of being shared and becoming a common value. Durkheim claimed that subjects were ruled by society and suggested a double identity for man: the first being an identity at the individual level and the second as part of society. Suicide, according to the Author, is the result of the disruption of the subject's social integration related to various factors and he acknowledges four kinds of suicide, namely altruistic, egoistic, fatalistic and anomic suicide (Durkheim, 1897).

A new conceptualization of suicide within economies of power: Duerkheim influence
Durkheim's structural approach to suicide together with his sociological theories profoundly influenced French Structuralism and led to the development of a complex conceptualization of suicide that implied a three-level analysis of the act. The over-structural level considered social and political ideologies and religion; the structural level included social class, communities and economic and political aspects; the under-structural level in which individual and social psychological aspects were considered.

None of them could stand alone, but each of them had to be analyzed for the whole understanding of the phenomenon.

To gain a deeper understanding of the sociological processes described above which led to a change in the conceptualization of suicide, Foucault's (1981) concept of differing "economies of power" (p.135) could be helpful. According to Foucault's analysis, there were two contrasting "economies of power" (p. 135) namely "sovereign power" and "bio-power". The former referred to the privilege of sovereigns to dispose of their subjects' life, they could either "*take* their life or *let* them live" (Foucault, 1981, p.136). According to the "sovereign-power" perspective, when suicide was committed the victim had stolen his own life and the right to decide over it from the sovereign and consequently had to be punished and to pay back for this crime with the confiscation of goods and the denial of a Christian burial. In the seventeenth and eighteenth centuries, a shift within society occurred and the exercise of power became an effort to reinforce, control, optimize and organize life-generating forces rather than submitting to and impeding them. This new form of power, called by Foucault "bio-power", was situated and exercised by society, i.e. at the level of life rather being somehow above it exercised by a sovereign or God (Rabinow and Rose, 2003). Its main aim was to foster life and maximize the potentialities of both the individual body and the body of the population, thus creating an "anatomo-politics of the human body" (Foucault, 2002, p.138) alongside a "biopolitics of the population" (ibid., p.139). Suicide, in this bio-political field, could become the target of management at both population and individual level. In this setting, suicide became a failure of society and led to the recognition of suicide as a problem, which had to be further investigated and better understood.

However, in both "economies of power" the subject was the focus of some form of pressure and control exerted by the society in which he/she lives (i.e., the subject played a passive role and was somehow shaped by society).

Since the early nineteenth century suicidal people were confined to asylums and the French and British began keeping track of suicides in order to expand the body of knowledge of this phenomenon (Hacking, 1990). These changes may have resulted from this new bio-political rationality and represent the forerunners of modern-day epidemiological studies and treatment strategies (Marsh, 2010). The problematization of suicide – which was not acknowledged as an inevitable death –led to many studies, which allowed a deeper understanding of suicide in its various aspects. In the twentieth century, "suicidology", i.e. a discipline of the scientific study of suicide (Maris et al., 2000), was developed. Since suicide is a complex phenomenon, suicidology involves many different fields and disciplines, the two primary ones being psychology and sociology (Shneidman, 2001).

Suicide and economic factors: some socioeconomic understandings from the past
Historians and sociologists investigated the effect of economic cycles on suicide rates, which to date remains uncertain (Stuckler et al., 2011). A large stream of empirical studies support the influence of unemployment on suicide rates in Europe (ibid.), suggesting an increase of unemployment by 1 percentage point would lead to an increase by 0,09 percentage point of suicide rate (per 100.000 inhabitants) (Breuer, 2015). This would peak by 0,21 percentage point considering men in working age (ibid.), though other studies do not confirm the existence of this influence (Fountoulakis et al., 2013; Polyzos, 2012; Andres, 2005). Considering other economic parameters, an increase in gross domestic product per capita (GDP) and gross value added (GVA) negative correlated with suicide rates in Europe (Breuer, 2015). An Italian study investigating

the relationship between inflation, employment status and suicidal behavior in a stratified sample showed that the unemployed were at higher suicide risk than the employed and in particular, this was higher in the unemployed who had been previously employed. The change in social status caused by the job-loss would have determined a further vulnerability to inflation in this sample compared with the unemployed who never worked and those employed (Solano et al., 2012). These recent studies show a complex interplay of socioeconomic factors in influencing suicidal behaviors which, however, is still an open question. Therefore, we aimed to review and discuss some sociological theories involving economic factors together with factors related to mental illness, which we believe should be carefully considered when discussing suicide.

From an economic point of view, when the terrors of death are less than the terrors of life, the cost/benefit equation increases suicide risk (Stack, 2000). People under high economic strain, such as the poor, face greater terror, and social support systems play a pivotal role in lowering suicide rates (Zimmerman, 1987a,b;1990;2002; Yur'yev, 2012). For instance, among the unemployed the prevalence of psychological problems is twice as high as in employed people (Paul and Moser, 2009) and unemployment had a lower impact in countries with strong employment protection. Conversely, lesser unemployment protection coupled with sharper increase in unemployment yield a strong unemployment effect on suicide (Norström, Grönqvist, 2015). Consequently, unemployment protection modifies the impact of unemployment on suicide rates. However, the scarce development of social support networks in the past, when the welfare state was not developed, should be carefully taken into account when considering suicide and economic regressions in the past (Yur'yev, 2012).

The economic uncertainty of the seventeenth and eighteenth centuries (Hoppit, 1986), that historians claim to be related to the rise of suicide rates, may be partly understood,

we believe, in the light of Durkheim's (1897) "anomic suicide" (ibid., p.241). This occurs when a man goes through extreme changes in wealth. Interestingly, this includes both economic ruin and windfall gains since in both cases previous expectations from life are brushed aside and new expectations must be found before the subject can judge his new situation in relation to the new limits. It is the rapid economic and social upheaval that causes a state of anomie regardless of the direction of the change (ibid.). For instance, the lack of definition that is typical of economic uncertainty is reflected both in stock market behavior and suicide rates (Pierce, 1967). Durkheim (1897) reported through the conceptualization of anomie – i.e., of unintegration- the 51% increase in suicide rates that occurred in Vienna from 1872 to 1874 during the economic crisis. During upheavals, society abruptly loses its normative and limiting function that regulates and shapes the subject's desires and needs from birth, causing a state of confusion in which the subject loses the perception of his role in society and is exposed to dysregulations leading to suicide. For instance, uncertainty and instability dominated the impressions of life in the Eighteen Century England during which harvest fluctuations or depressions in trade and fiscal crises could abruptly upset the welfare of the family (George, 1951). More than thirteen periods of financial crises are reported in the eighteenth century in England and among them the bursting of the South Sea Bubble was presumably the greatest one which caused an almost doubling of suicides in London the year after the crash (Hoppit, 1986) and the General Bills of Mortality 1660-1800 reported a period of high rates of suicides in the following two decades (Mac Donald, Murphy, 1990). Wealth and happiness were closely bound in the mind of seventeenth-eighteenth century men; the suicide of a wealthy man was reported by the newspapers of the time only as something understandable as an act deriving from insanity (Mac Donald and Murphy, 1990). Data from the King's Bench showed how the majority of suicide victims with a verdict of *felo de se* reported by coroners between 1485 and 1714

had a humble social status (Figure 2), this, however, could result from the need of wealthy people to save their goods from forfeiture thus needing a *non compos mentis* verdict (Houston, 2010).
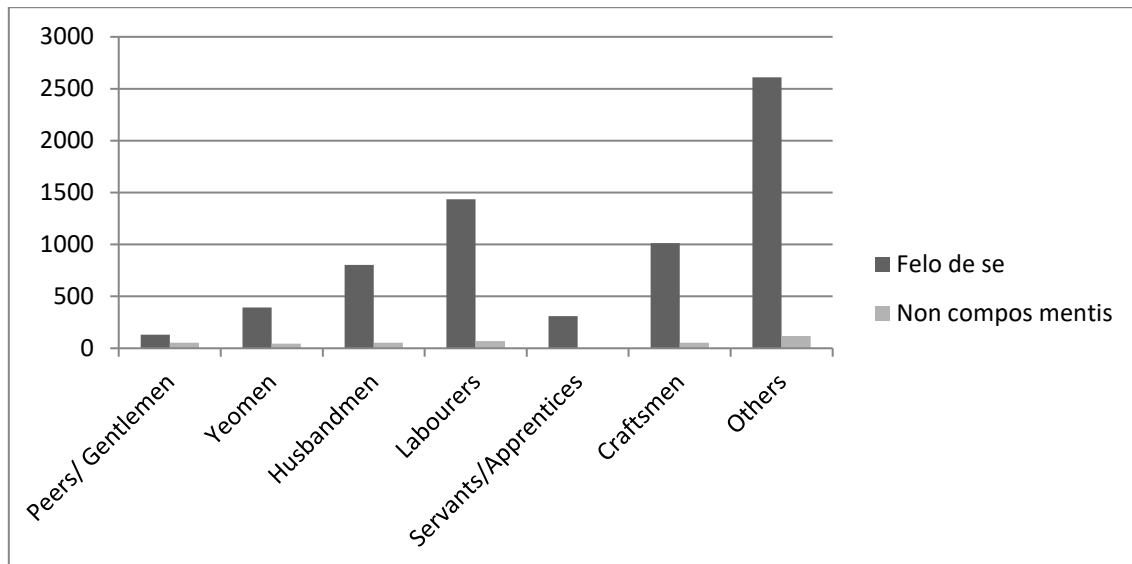
Figure 2. Social status and verdicts of suicides in England 1485-1714. These however, are absolute data and do not consider the different representation of social classes within the population. (Source: Public Record Office, adapted from Mac Donald Murphy, 1990)

However, the belonging of the majority of the victims to humble social classes, independently from the assigned verdict, may be understood also in the light of studies, concerning the relationship between poverty and mental illness, being the former either the social causation of the latter or its consequence (Costello et al., 2003; Gadalla et al., 2009). This is consistent with Halbwachs's conceptualizations (1930) that underlined the importance of isolation in causing suicide and maintained that suicide should be understood as resulting from the complex interplay of both socioeconomic and psychological personal factors.

Furthermore, Henry and Short (1954) suggested that suicide may be an act of aggression and linked it with frustration, i.e., an economic crisis would be associated with a high degree of frustration due to changes in hierarchical positions that together with external

restrictions and disappointment of expectations would cause suicide. However, not all studies supported Henry and Short's theory and only few found any relationship between integration, regulation and suicide in primitive societies (Lester, 1968;1992). Durkheim's theory could be successfully applied to individual cases, though it would fail to explain the variation in suicide rates of societies. Gibbs and Martin (1958) further developed the Durkheimian approach by suggesting the notion of "status integration" (p.140), i.e., the integration of the different roles the individual occupies at the same time in society. Suicide could be caused by the simultaneous presence of incompatible statuses and their sudden change, as occurs in an economic crisis. Thus, macro and micro economy are intertwined in influencing suicidal behaviors.

Hamermesh and Soss (1974) were the first to develop an economic theory for suicide in which living conditions, such as income, status and unemployment would explain suicidal behavior and supported it providing empirical data. They postulated the existence of a direct relationship between certain economic factors both pecuniary and not – such as permanent income and discounted lifetime utility – and the likelihood of suicide of a certain subject. According to the economic theory of suicide an individual (*i*) at age (*a*) with a permanent income (*Y)* takes his own life when the total discounted lifetime utility (Z_i) plus the individual's taste for living ($b_i)$ reaches zero.

$$Z_i\,(a,Y) + b_i \;\; = \;\; 0$$

with

$$Z_i(a, Y) = \int_a^\omega e^{-r(m-a)} U_m P(m) dm$$

where ω denotes the highest attainable age, *r* the discount rate and *Um* the expected utility at age *m*. *Pm* is the probability of survival to age *m* given survival to age *a*. In addition to its negative relationship with the age m, the individual's expected utility *Um*

is positively related to the permanent income *Y*. The individual's taste for living *bi* is assumed to be normally distributed so that the age- adjusted aggregate suicide rate, defined as the fraction of individuals in the age group *a* for whom *Z(a, Y)* reaches –*b*, is inversely related to the permanent income Y. Therefore, the economic theory of suicide suggests that the increase in income pro capita leads to a reduction of the likelihood of suicide.

Though suicide derives from the intertwining of different factors, the economic theory of suicide is noteworthy since it represents the first attempt economists did to investigate suicide from their point of view.

Conclusion

In this study, we provided different views of past conceptualizations of suicide concerning both its social value and its interplay with economic factors and how this changed throughout time. Suicide is a complex and difficult-to-explain phenomenon for which many hypotheses and theories have been suggested, though no definitive one has been found yet. "Struggling to make sense of a phenomenon is something about which we can do a great deal" (Berman, 2012) and we believe that keeping in mind the past could provide a valuable background for a deeper understanding of the present. This could lead to the development of more effective prevention strategies, such as better social support structures and to a deeper awareness of the importance of social support programs in times of uncertainties especially for the poor. This we believe to be of paramount importance considering a time in which cuts on expenditure are being made and exceeding reduction of social support programs might put too much strain on vulnerable people.

Temperaments, coping strategies and attitude towards suicide An investigation among medical students

Introduction

Contemporary psychiatry recognized the growing relevance of pervasive characteristics underlying severe suicidal behaviors as well as showed the importance of affective temperaments together with coping strategies in favoring the possible development of psychiatric disorders and at risky behaviors (Akiskal et al., 2005; Tondo et al., 2018). In particular, a large body of literature reported the association between cyclothymic, depressive, anxious, irritable temperaments based on assessment with the Temperament Evaluation of Memphis, Pisa, Paris and San Diego-autoquestionnaire version (TEMPS-A) and higher risk of suicidal behaviors (Pompili et al., 2012; Baldessarini et al., 2016); differently, the hyperthymic temperament seems to exert a protective effect against suicidal behavior (Tondo et al., 2018; Vázquez et al., 2018). Interestingly, affective temperaments remain stable over time and are commonly identifiable during the early age both in clinical and not clinical populations (Mitsui et al., 2017; Vázquez et al., 2018).

Moreover, coping strategies have been recognized as important factors in promoting and protecting against suicidal behavior both before and after a positive history of prior suicide attempts in different age groups and both clinical and non-clinical samples (Knafo et al., 2015; Mirkovic et al., 2015; Imran et al., 2016). For instance, Heffer and Willoughby (2017) analyzed the role of coping strategies in developing depressive symptoms and suicidal ideation among university students through a two level analysis in which they investigated either the number of coping strategies employed by each student and the frequency of their use. Negative coping strategies were associated with

higher risk of developing depressive symptoms and suicidal ideation both in respect to their number and frequency of use (Heffer and Willoughby, 2017). Interestingly, the subject's coping flexibility that is the possibility of using different types of positive coping strategies – e.g., both problem-focused and emotional-focused coping strategies was associated with better psychosocial adjustment, whereas the massive use of the same positive coping strategies did not confirm this result (Heffer and Willoughby, 2017). Furthermore, evidence suggests that different attitudes towards suicidal behavior play a significant role in the self- and others' suicidal behaviors though contrasting evidence have been reported to this regard (Domino, 2015; Anderson et al., 2008; Li et al., 2010; Kodaka et al., 2011; Galynker et al., 2015; Li et al., 2015; Patel et al., 2016). Moreover, depressive symptoms and suicidal ideation that have been estimated to be 50% and 10% - 11.1%, respectively, among medical students (Dyrbye et al., 2008; Rotenstein et al., 2016).

This study aims at investigating the association between severe suicidal thoughts and behaviors, coping strategies, temperament and attitude towards self- and others' suicidality in a sample of medical students. To do so, we investigate the role of affective temperaments in predicting coping strategies and attitudes toward suicide in a sample of medical students who displayed severe suicidal thoughts and behaviors compared to those with no severe suicidal thoughts and behaviors. Moreover, the interplay of affective temperaments and coping strategies in determining attitudes toward self- and other's suicidal thoughts and behaviors has been explored.

The following hypothesis were investigated:

-Depressive and cyclothymic temperament and maladaptive coping strategies are more likely to be associated with greater empathy towards self and others' suicidal behavior

and are more common in the severe suicidal thoughts and behaviors group compared to the no severe suicidal thoughts and behaviors group.

-no severe suicidal thoughts and behaviors group shows higher judgmental attitudes towards self- and others' suicidal behavior, better adaptive coping strategies, and higher hyperthymic temperament compared with the severe suicidal thoughts and behaviors group.

Methods

This is a naturalistic cross-sectional study in which participants were recruited using a sample of medical students attending the first to fourth year of the School of Medicine, University of Genoa. Students attending the fifth and sixth year were not included in the survey because they have already attended the course of psychiatry and we suppose that this may have influenced their attitudes and general perception towards suicidal behavior. The permissions to proceed were obtained by the Dean of the School of Medicine while the survey was carried out anonymously in order to preserve the confidentiality of the participants' responses. Prior to completing the survey, each student signed an informed consent that explained in detail the nature and purpose of our research and allowed the analysis and use of their responses for research aims.

Students had to be within the age range 18 to 26 while surveys of students out of this age range were not included. Moreover, surveys in which the students missed more than one question concerning the direct/indirect involvement in suicidal behavior were not included in the sample. On this basis, a final sample of 522 surveys out of a total of 531 was deemed valid and consequently analyzed. In particular, 6 surveys were not included in the final sample because more than one item concerning the subject's direct/indirect

involvement in suicidal behaviors were missing and 3 surveys were not included because the subjects were older than 26. All individuals accepted voluntarily to participate in the study and provided their written informed consent.

2.1 Materials

Each survey consisted of a socio-demographic form, the Suicide Opinion Questionnaire (SOQ) (Domino et al., 1980), the Coping Orientation to Problem Experienced (COPE) (Carver et al., 1989) and TEMPS-A (Akiskal et al., 2005; Pompili et al., 2008).

The demographic form inquired about age, sex, siblings, type of high school, home location (e.g., rural, urban or suburban), level of academic achievement (measured as being late with their courses), presence of projects for their future (measured as the students' plans for their after-graduation studies and future kind of medical profession), presence of parents working in medical or mental health environment. Parents working in medical or mental health fields may influence the subject's understanding and perception of suicide- related phenomena by possibly providing specific knowledge about mental illness and different attitudes towards it.

The TEMPS-A is a questionnaire designed to evaluate the fundamental affective temperaments: depressive, cyclothymic, hyperthymic, irritable, and anxious temperament (Akiskal et al., 2005; Pompili et al., 2008). Recent evidence indicated that most studies support a five factor solution while different versions of the TEMPS-A have adequate internal consistency and reliability (Elias et al., 2017).

Participants were also asked to complete the Coping Orientation to Problem Experienced Questionnaire (COPE) (Carver et al., 1989). that is a self-report questionnaire that measures 15 coping strategies, i.e, five scales that measure problem-focused coping; six scales that measure emotion-focused coping; four scales that measure potentially dis-adaptive strategies/less useful coping responses such as denial,

behavioral disengagement (i.e., reducing one's effort to deal with the stressor, even giving up the attempt to attain goals with which the stressor is interfering, is reflected by phenomena that are also identified with terms such as helplessness and occur when people generally expect poor coping outcomes); mental disengagement (i.e., a variation on behavioral disengagement, postulated to occur when conditions prevent behavioural disengagement and occur via a wide variety of activities such as daydreaming and escaping through sleep, TV, or videogames) and alcohol/drug disengagement.

Moreover, the COPE may be used as a measure of dispositional coping or a situational measure of coping with a specific stressful event.

The Suicide Opinion Questionnaire (SOQ) (Domino et al., 1980) consists of 107 items, 100 attitudinal in nature, and 7 demographic items. For the attitudinal items, the respondent is asked to use a five-point Likert response scale with options ranging from strongly agree, agree, undecided, disagree, and strongly disagree with these options that are scored on a scale from 5 for strongly agree to 1 for strongly disagree. The SOQ items cover a wide variety of opinions related to suicide and parasuicide, most of which are attitudinal in nature. The five factor SOQ scale (SOQ-F). has been used to analyze the responses that identifies five dominions, namely (a) acceptability, (b) perceived factual knowledge, (c) social disintegration, (d) personal defect, and (e) emotional perturbation. Psychometric studies provided support for this 5-factor structure with Cronbach alpha reliabilities ranging from .60 to .89 (Rogers and DeShon, 1995). SOQ has been used in a large number of research studies in the past, and it remains the most widely used questionnaire assessing opinions about suicide (Anderson et al., 2008). The SOQ cross-cultural applicability has been shown by different studies (Domino, 1981; Domino et al., 2000; Domino et al., 2001-2002; Domino, 2005) including Italian samples (Domino and Perrone, 1993).

2.2 Procedure

Participants accepted voluntarily to take part into the survey and the study design was approved by the local Ethical Review Board of the School of Medicine, University of Genoa. The projected time of administration and completion of the survey was approximately 30 minutes but they had all the necessary time available to carry out the survey as there were no right or wrong answers. Moreover, students were asked to use either black or blue pens to fill the forms in order to make their own survey less recognizable.

The surveys were administered during their class period over the course of two months and the filled up surveys were collected in boxes that were opened up and analyzed only at the end of the administration study phase in order to further assure confidentiality.

Two groups were identified within the sample, i.e. subjects with severe suicide thoughts and behaviors, namely the severe suicidal thoughts and behaviors group and subjects with not severe suicide thoughts and behaviors, namely the no severe suicidal thoughts and behaviors group (NSSTB) according to the subjects' responses to the SOQ items 104 "Have you ever seriously considered suicide?" and 105 "Have you ever attempted suicide?". Subjects who responded positively to one or both items were put into the sub-group severe suicidal thoughts and behaviors and the others in the sub-group no severe suicidal thoughts and behaviors.

2.3 Statistical analysis

The socio-demographic and clinical characteristics of the subjects were represented as mean and standard deviation (SD) for continuous variables or in terms of frequency and percentages regarding categorical variables.

In order to analyze differences between the severe suicidal thoughts and behaviors and no severe suicidal thoughts and behaviors group, we used the Pearson $\chi 2$ test with Yates correction or with Fischer exact test for the comparison of categorical variables, and *t*-test for independent samples for continuous variables. We also divided our sample in three subgroups /suicide ideation vs suicide attempt vs no suicide behavior) and we used the Pearson $\chi 2$ test for categorical variables and ANOVA for the continuous variables. Logistic regression analysis was used to explore the relationship between subjects with severe suicidal dimensions (severe suicidal thoughts and behaviors group) and each of the other independent variables previously found associated in the statistical analyses. The probability of entering the equation was set at $p < 0.05$.

All statistical analyses were performed using SPSS version 20.0 (SPSS Inc., Chicago) and the value of statistical significance was set at $p < 0.05$.

Results

Six hundred thirty-four (N=634) questionnaires were prepared according to the official numbers of students attending the first to the fourth year of course in Medicine and Surgery at the University of Genoa. Five hundred fifty-six (N=556) questionnaires were distributed during the study time frame. Seventy-eight (N=78) questionnaires were not distributed and may be those of students who have abandoned their studies without having informed the University central offices yet, be abroad for some months to study or other not specified reasons. No students were on maternity leave or sick for periods longer than two weeks during the study time-frame according to the university official registers. Eight (N=8) questionnaires were not returned to the research group, one (N=1) appeared seriously damaged as to impair the possibility of its interpretation, twenty three (N=23) were completed not properly (two answers given for the same item; at least one

of the suicide-related questions not answered; comments written on the questionnaires that may have impaired the individual's confidentiality), two (N=2) were returned with the students' name and could not be used to preserve the students' confidentiality. Five hundred fifty-two (N=522) questionnaires were included in the study, i.e. 82,3% of officially registered students in the investigated years of Medicine and Surgery course at the University of Genoa. The mean (±SD) age of the sample was 23.6 (±1.1) years and 41.0*%* students were males.

In addition, 47.7% of the sample had good academic achievement and 29.9% had active projects for the future (Table 1). 72,4% of the subjects had siblings and formed the 75.1% of the no severe suicidal thoughts and behaviors and the 59,1% of the severe suicidal thoughts and behaviors. 52.9% of the sample live in urban places and represent the 48,9% of the severe suicidal thoughts and behaviors and the 53,7% of the no severe suicidal thoughts and behaviors (Table 1). Students belonging to the severe suicidal thoughts and behaviors group were 20.3% of the whole sample; males were 58.0% and 37.6% of the severe suicidal thoughts and behaviors and no severe suicidal thoughts and behaviors group respectively (Table 1).

Tab. 1. Socio-demographic data and chi-square test of socio-demographic data and the SS, NSS groups.

	Total sample (N=522)	SS group (N=88)	NSS group (N=434)	X^2	df	p
Gender, N (%)						
Male	214 (41.0%)	51 (58.0%)	163 (37.6%)	12.584	1	< .001
Female	308 (59.0%)	37 (42.0%)	271 (62.4%)			
Age, mean ± SD	23.62 ± 1.10	23.60 ± 1.11	23.62 ± 1.10	.154	520	.878

					df	p
Siblings, N (%)	378 (72.4%)	52 (59.1%)	326 (75.1%)	9.405	1	**.002**
High School, N (%)						
Classic	164 (31.4%)	25 (28.5%)	139 (32.0%)	.746	2	.585
Scientific	349 (66.9%)	61 (69.3%)	288 (66.4%)			
Linguistic	9 (1.7%)	2 (2.3%)	7 (1.6%)			
Good Accademic Achievements	249 (47.7%)	23 (26.1%)	226 (52.1%)	19.730	1	<**.001**
Projects for the future	156 (29.9%)	19 (21.6%)	137 (31.6%)	3.475	1	.062
City Living Place, N (%)	276 (52.9%)	43 (48.9%)	233 (53.7%)	.683	1	.409
Nationality, N (%)						
Italian	512 (98.1%)	88 (100.0%)	424 (97.7%)	2.067	1	.150
Other	10 (1.9%)	0 (0.0%)	10 (2.3%)			

The chi-square test showed that subjects belonging to the severe suicidal thoughts and behaviors group were more likely to be males (p<.001), only children (p=.002), with poor academic achievement (p<.001), and less likely to have a parent working in medical or mental health fields (p<.001). No significant association was reported between severe suicidality and "the presence of projects for their future" (measured as the students' plans for their after-graduation studies and future kind of medical profession) (p=.062) and home location (p=.409) (Table 1).

Fisher's exact test showed significant associations between belonging to the severe suicidal thoughts and behaviors group anxious (p=.001) and cyclothymic (p=.032)

temperament. Conversely, hyperthymic and depressive temperaments were significantly associated with the no severe suicidal thoughts and behaviors group (p<.001 and p=.049 respectively) (Table 2a).

Tab. 2a. Fischer exact test evaluating the relationship between temperaments (TEMPS-A) and the severe suicidal thoughts and behaviors and no severe suicidal thoughts and behaviors group

	Severe suicidal thoughts and behaviors group (N=88)	No severe suicidal thoughts and behaviors group (N=434)	X^2	p
Depressive, N (%)	13 (14.8%)	106 (24.4%)	3.87	**0.049**
Cyclothymic, N (%)	17 (19.3%)	48 (11.1%)	4.58	**0.032**
Hyperthymic, N (%)	15 (17.0%)	202 (46.5%)	26.21	**<0.001**
Irritable*, N (%)	1 (1.1%)	3 (0.7%)	.19	0.523
Anxious, N (%)	48 (54.5%)	151 (34.8%)	12.10	**0.001**

df=1 for all mentioned temperaments

*Fischer exact test

On table 2b the relationship between temperaments (TEMPS-A) and the three subgroups (suicide ideation vs suicide attempt vs no suicide) is presented.

Tab. 2b. Chi-square test evaluating the relationship between temperaments (TEMPS-A) and the three subgroups (suicide ideation vs suicide attempt vs no suicide).

	SI group (N=46)	SA group (N=42)	No severe suicidal thoughts and behaviors group (N=434)	X^2	p
Depressive, N (%)	6 (13.0%)	7 (16.7%)	106 (24.4%)	4.04	0.133
Cyclothymic, N (%)	13 (28.3%)	3 (7.1%)	48 (11.1%)	12.55	**0.002**
Hyperthymic, N (%)	7 (15.2%)	8 (19.0%)	202 (46.5%)	26.34	**<0.001**
Irritable, N (%)	0 (0.0%)	1 (2.4%)	3 (0.7%)	1.83	0.401
Anxious, N (%)	24 (52.2%)	24 (57.1%)	151 (34.8%)	12.33	**0.002**

Perceiving suicide as the result of a personal defect was significantly associated with the severe suicidal thoughts and behaviors group (p<.001) while the no severe suicidal thoughts and behaviors group was significantly associated with higher rates of acceptance of self and others' suicidal thoughts and behaviors (p<.001) and were more likely to link suicidal behavior with emotional perturbation (p=.003) (Table 3a).

Tab. 3a. Relationship between Attitudes towards Suicide (SOQ), COPE and the severe suicidal thoughts and behaviors and no severe suicidal thoughts and behaviors group

mean ± SD	Severe suicidal thoughts and behaviors group (N=88)	No severe suicidal thoughts and behaviors group (N=434)	X^2/t	p
Acceptability	32.2 ± 6.5	38.3 ± 5.3	9.37	**<0.001**
Social Disintegration	36.5 ± 3.8	36.6 ± 3.8	.21	0.836
Emotional Perturbation	19.7 ± 3.6	20.7 ± 2.8	3.02	**0.003**
Perceived Factual Knowledge	33.7 ± 3.5	33.6 ± 3.4	-.25	0.800
Personal Defect	40.3 ± 6.6	37.7 ± 4.6	-4.41	**<0.001**
Problem-focused coping Active coping Planning Suppression of competing activities Restraint coping Use of instrumental social support	10.8 ± 2.3 11.5 ± 3.2 9. 6 ± 1.5 9.8 ± 2.2 11.4 ± 2.1	12.2 ± 1.6 12.8 ± 2.4 10.2 ± 2.0 10.0 ± 2.0 11.8 ± 2.4	6.86 4.28 2.85 .74 1.09	**<0.001** **<0.001** **0.005** 0.462 0.275

Emotion-focused coping				
Use of social-emotional support	10.3 ± 3.0	11.3 ± 3.1	2.66	**0.008**
Positive reinterpretation and growth	11.6 ± 2.1	12.3 ± 2.0	3.04	**0.002**
Acceptance	10.4 ± 2.9	11.2 ± 2.3	2.97	**0.003**
Humor	7.8 ± 2.6	7.4 ± 2.5	2.92	0.168
Venting of emotions	10.7 ± 2.6	9.9 ± 2.8	-2.25	**0.025**
Turning to religion	6.5 ± 2.8	6.4 ± 3.3	-.16	0.876
Potentially disadaptive strategies				
Denial			-4.27	
Behavioral disengagement	6.3 ± 2.5	5.4 ± 1.8	-8.51	**<0.001**
Alcohol and drug disengagement	8.3 ± 2.7	6.3 ± 1.8	-7.26	**<0.001**
Mental disengagement	6.3 ± 3.0	4.7 ± 1.5	-6.47	**<0.001**
	10.3 ± 2.3	8.6 ± 2.2		**<0.001**

df=520 for all mentioned items

The severe suicidal thoughts and behaviors group showed significant association with lower problem-focused and emotional-focused coping strategies, i.e. active coping strategies (p<.001), lower planning (p<.001), suppression of competing activities (p=.005), venting of emotions (p=.025), use of social support (p=.008), positive reinterpretation and growth (p=.002), and lower acceptance (p=.003). Conversely, the severe suicidal thoughts and behaviors group compared to the no severe suicidal thoughts and behaviors group showed strong significant associations with all the subscales of the potentially dis-adaptive coping strategies scale, i.e. denial (p<.001), mental and behavioral disengagement (p<.001), alcohol and drug disengagement (p<.001) (Table 3a).

On table 3b the relationship between attitudes towards suicide (SOQ) and COPE among the three subgroups (suicide ideation vs suicide attempt vs no suicide) is presented.

Tab. 3b. Relationship between Attitudes towards Suicide (SOQ) and COPE among the three subgroups (suicide ideation vs suicide attempt vs no suicide).

mean ± SD	SI group (N=46)	SA group (N=42)	No severe suicidal thoughts and behaviors group (N=434)	F	p
Acceptability	34.7 ± 7.0	29.5 ± 4.6	38.3 ± 5.3	55.61	**<0.001**
Social Disintegration	36.3 ± 3.9	36.6 ± 3.7	36.6 ± 3.8	0.08	0.926
Emotional Perturbation	19.2 ± 3.2	20.3 ± 3.9	20.7 ± 2.8	6.13	**0.002**
Perceived Factual Knowledge	33.7 ± 2.5	33.7 ± 4.4	33.6 ± 3.4	0.03	0.969
Personal Defect	40.6 ± 4.6	39.9 ± 8.2	37.7 ± 4.6	9.90	**<0.001**
Problem-focused coping					
Active coping	10.2 ± 2.2	11.4 ± 2.4	12.2 ± 1.6	29.10	**<0.001**
Planning	10.7 ± 2.6	12.4 ± 3.6	12.8 ± 2.4	14.20	**<0.001**
Suppression of competing activities	9.1 ± 1.8	10.1 ± 0.8	10.2 ± 2.0	7.15	**0.001**
Restraint coping	9.2 ± 1.4	10.5 ± 2.6	10.0 ± 2.0	5.04	**0.007**
Use of instrumental social support	11.0 ± 2.0	11.9 ± 2.2	11.8 ± 2.4	1.95	0.143
Emotion-focused coping					
Use of social-emotional support	11.2 ± 2.8	9.3 ± 3.0	11.3 ± 3.1	7.95	**<0.001**
Positive reinterpretation and growth	11.8 ± 1.7	11.4 ± 2.5	12.3 ± 2.0	5.24	**0.006**
Acceptance	10.6 ± 2.3	10.1 ± 3.4	11.2 ± 2.3	4.77	**0.009**
Humor	6.5 ± 2.1	9.3 ± 2.2	7.4 ± 2.5	15.36	**<0.001**
Venting of emotions	11.1 ± 2.9	10.2 ± 2.1	9.9 ± 2.8	3.78	**0.023**
Turning to religion	6.5 ± 3.0	6.5 ± 2.5	6.4 ± 3.3	0.01	0.987
Potentially disadaptive strategies					
Denial	6.8 ± 2.5	5.9 ± 2.4	5.4 ± 1.8	11.59	**<0.001**
Behavioral disengagement	7.8 ± 2.1	8.8 ± 3.1	6.3 ± 1.8	38.80	**<0.001**
Alcohol and drug disengagement	6.8 ± 3.2	5.7 ± 2.6	4.7 ± 1.5	30.49	**<0.001**
Mental disengagement	10.0 ± 2.6	10.5 ± 1.8	8.6 ± 2.2	21.39	**<0.001**

Logistic regression showed a positive correlation between the severe suicidal thoughts and behaviors group and the following variables: siblings (p=.009), academic insuccess (p=.004), personal defect (p<.001), suppression of competing activities (p=0.001), venting of emotions (p=.037), mental and behavioral disengagement (p=.006 and p= .031 respectively), and male sex (p=.006) (Table 4).

Table 4. Logistic regression analysis (R^2 Cox-Snell: .424; R^2 Nagelkerke: .711) of socio-demographic variables, coping strategies (COPE), temperaments (TEMPS-A), attitudes towards suicide (SOQ) in the severe suicidal thoughts and behaviors and no severe suicidal thoughts and behaviors group.

Variables	E.S.	Wald	p	Odd Ratio	95%CI
Emotional Perturbation	.103	31.058	**<0.001**	.752	.614-920
Anxious temperament	.715	.312	**<0.001**	.671	.165-2.723
Acceptance	.110	14.028	**<0.001**	.874	.534-.822
Suppression of competing activities	.135	10.322	**0.001**	1.014	1.277-2.744
Good Academic Achievements	.550	8.127	**0.004**	4.802	1.633-14.123
Planning	.203	.011	**0.004**	.560	.376-.833
Mental disengagement	.143	7.705	**0.006**	1.489	1.124-1.972
Gender	.561	7.568	**0.006**	4.689	1.565-14.098
Acceptability	.061	30.328	**0.006**	.714	.633-.805
Siblings	.576	6.912	**0.009**	4.543	1.470-14.043
Use of social-emotional support	.116	5.642	**0.018**	1.872	.604-.953
Behavioral disengagement	.145	4.679	**0.031**	1.369	1.030-1.819

Venting of emotions	.117	4.370	**0.037**	.662	1.015-1.609
Depressive temperament	.706	.551	0.163	1.689	.423-6.746
Cyclothymic temperament	.834	1.946	0.283	.312	.061-1.602
Hyperthymic temperament	.752	1.155	0.577	2.244	.514-9.807
Denial	.179	3.821	0.051	1.278	.496-1.001
Age	.204	3.751	0.053	1.485	.995-2.216
Positive reinterpretation and growth	.139	.938	0.333	.759	.666-1.148
Alcohol and drug disengagement	.143	.015	0.903	.983	.743-1.300
Personal Defect	.066	8.176	0.916	1.448	1.271-1.650
Constant	7.266	.760	.383	.002	

df=1 for all mentioned items

Discussion

Overall, our results show that students who experienced suicidal thoughts and behaviors used more often not only maladaptive and rigid coping strategies leading to mental and behavioral disengagement but were also more likely to be not empathetic towards self- and other's suicidal behavior. For instance, students who experienced suicidal thoughts and behaviors showed more judgmental attitudes towards individuals with suicidal thoughts and behaviors and tended to judge them as "weak" subjects.

These findings showed us how the lived experience of serious suicidal wishes and behaviors does not prompt to deeper and more empathetic understanding of these characteristics in others on the basis of human sharing that cannot be accessed by these subjects apparently. In particular, the use of maladaptive coping strategies such as poor venting of emotions together with mental and behavioral disengagement may foster subjects' isolation and retreat from social relationships along with detachment from self and others' emotional experience, thereby favoring the development of judgmental attitudes in this population. Moreover, students who had suicidal thoughts and behaviors were more likely to have anxious and cyclothymic temperaments. These temperaments play a significant role in the development of impulsive behaviors, related to attentional

and motor impulsivity (Beşirli, 2018). Subjects with these temperaments may be more likely in structuring maladaptive coping strategies.

One fourth of our sample had severe lifetime suicidal thoughts and behaviors and males were more likely to experience them. These findings are consistent with previous evidence showing suicidal thoughts and behaviors in medical (Rotenstein et al., 2016; Blacker et al., 2018) and college students in general with higher rates among males with poor academic performance (Mortier et al., 2018a,b).

Interestingly, our results showed that depressive and hyperthymic temperaments were more common in the no severe suicidal thoughts and behaviors group. The higher presence of the hyperthymic temperament in the no severe suicidal thoughts and behaviors group was consistent with the findings reported by Pompili et al. (2013) showing the long-term predictive role of the hyperthymic temperament with respect to health and social functioning as this temperament provides greater energy, ambition, drive, confidence, cheerfulness, gregariousness, sociability, optimistic attitude together with increased creativity and social skills.

Our results do not confirm previous evidence reporting significant associations between depressive temperament and higher suicide risk (Pompili et al., 2012; Vasquez et al., 2018) which has been even confirmed by existing neurobiological and genetic findings (Serafini et al., 2010; Gonda et al., 2011). . This may be related to the different study samples as the latter studies have been specifically conducted among subjects with specific psychiatric conditions such as mood disorders while our study mainly referred to a non-clinical sample (Karam et al., 2015). Moreover, our findings regarding the significant association between anxious/cyclothymic temperaments and higher suicidal

behavior are consistent with previous studies sustaining that these affective temperaments are more frequent in subjects with family history of completed suicide in first and second-degree relatives (Rihmer et al., 2013; Tanabe et al., 2016).

These findings comprehensively addressed the different attitudes according to which medical students have towards suicidal behavior according to their personal experiences of self and others' suicidality. For instance, students who seriously considered attempting suicide or had already attempted it, showed less empathetic attitudes towards self- and others' suicidal behavior. Students in the severe suicidal thoughts and behaviors group tended to perceive suicidal behavior as resulting from an inacceptable personal defect rather than understanding it according to an emotional perturbation as those in the no severe suicidal thoughts and behaviors group did. Similarly, Wallin and Runeson (2003) showed that students who had previous suicidal thoughts had greater difficulties in understanding the needs of suicidal individuals and had poor empathetic contact with them. Moreover, our results investigated the basis of these attitudes by analyzing the coping strategies used by students in the severe suicidal thoughts and behaviors groups who had greater cognitive rigidity with poor problem-solving focus and integrative capacities.

Severe suicidal thoughts and behaviors subjects were more likely to develop potentially dis-adaptive coping strategies such as denial, mental and behavioral disengagement, alcohol and drug disengagement together with suppression of competing activities and emotional venting. These results are consistent with previous evidence concerning the existence of cognitive distortions/deficits in suicidal subjects that may significant hamper the subjects' possibility of coping with intense emotional perturbation and develop sufficiently adaptive and integrated adjustments patterns (Turecki and Brent,

2016; Fazakas-DeHoog et al., 2017; Flink et al., 2017). In particular, behavioral disengagement implies that subjects give up even the attempt to attain goals with which the stressor is interfering.

Moreover, Panek et al. (2015) underlined the role of personal (also genetic) and environmental factors in determining strategies of coping with stress and temperamental traits according to the Regulative Theory of Temperament. These understandings further support our results showing the role of lived experience in mediating complex temperamental and coping factors. Similarly, Gould and colleagues (2018) showed that high school students exposed to negative life events had significant more maladaptive coping strategies with low help-seeking behaviors and high behavioral disengagement compared with students who never experienced negative stressful life events Interestingly, a large body of literature confirmed the association between maladaptive coping patterns, stressful life-events, suicide attempts, and suicidal ideation both in clinical and non-clinical samples (Pompili et al., 2011; Woodhead et al., 2014; Kattimani et al., 2015; Al-Gamal et al., 2016; Ambrus et al., 2017; Gould et al., 2018; Horwitz et al., 2018; Lamis et al., 2018).

This survey needs to be interpreted in the light of several limitations and strengths. The major shortcomings of the present study involve those entailed in surveys that use self-reporting questionnaires as their reliability could be biased by under-reporting, under-estimating and misunderstanding the issues. In particular, students with life experience of suicidal thoughts and behavior may have been more reluctant to take part in the study or give only partial answers to the suicide-related items, thus providing questionnaires that could be not included in the survey.

However, the operative definition of "severe suicidal thoughts and behavior", that we used, may overestimate the frequency and seriousness of suicidal thoughts due to self-

rating biases. In particular, the severe suicidal thoughts and behaviors and no severe suicidal thoughts and behaviors groups were formed according to the students' answer to the item 104 and 105 of the SOQ. These items are quite broad and may include different types of suicidal thoughts and behaviors entailing a variable severity of the suicidal behavior. In particular, subjects' personal understandings of "seriously considering suicide" and "having attempted suicide" are involved. In this sense, our groups encompass a wide range of suicide-related features in a non-clinical sample with the aim of investigating how the subjective experience of suicide – understood as having seriously considered suicide and/or having attempted suicide- may be related to temperamental factors.

We also aimed to find possible similarities in the subject's coping strategies and attitudes towards self- and others' suicidal thoughts and behaviors. Thus, our results did not include the investigation of these patterns among suicide ideations vs. suicide attempters which is beyond the scopes of the present study. Future studies should investigate and compare these patterns in these sub-populations of medical students. Moreover, the cross-sectional nature of this survey did not allow any inference concerning causality although providing preliminary evidence regarding the possible prediction of certain patterns involving affective temperaments, coping strategies, together with their role in shaping the subjects' attitudes towards suicidal behavior. We are aware of the complex interplay of multiple factors in causing suicidal behavior. Thus, we do not claim to explain such multifaceted dimension simply reducing it to temperamental and coping factors. Rather, we believe and hope that our understandings shedding light on specific patterns -associated with severe suicidal behavior in young adulthood may be helpful to implement effective prevention strategies aimed to improve emotional adjustment in the investigated population.

Further studies are needed to replicate our results in larger samples, with specific regard to the possible role of anxious and cyclothymic temperaments in the development of disruptive coping strategies leading to poor empathetic attitudes towards self and others' suicidal behavior.

However, one of the most relevant strengths of the present study includes the investigated sample which is relatively large and representative for the student population attending the School of Medicine of the University of Genoa for the considered years of course. To the best of our knowledge, no previous study investigated the complex interplay between affective temperaments, coping strategies, and attitudes towards suicide in medical students according to their personal experience of suicide thoughts and behaviors; therefore, our results could be of interest both when considering suicidal dimensions in medical students and in respect to their future behavior as clinicians when approaching and working with suicidal patients.

RESEARCH AREA B

NEUROBIOLOGY

OF

THE BRAIN

2. From mind to metabolism: lethality of suicide attempts and metabolic parameters a case- control investigation

Introduction

Suicide and nonfatal suicidal behaviors are major causes of mortality and morbidity worldwide. The Word Health Organization (WHO, 2014) estimated that approximately 800,000 people die from suicide each year and a number from ten to twenty times higher of individuals attempt suicide, indicating that both suicide and non-fatal suicidal behaviors need to be addressed as a real health priority. Variability in rates of suicidal behaviors within and between countries has been attributed to both population and individual risk factors, including economic status and cultural differences (WHO, 2017) that may significantly affect suicide risk.

Different explanatory models were developed in order to reveal the complex interplay between neurobiological factors such as genetic risk factors, altered serotoninergic functioning, and stress responses potentially leading to suicidal behaviors (Mann JJ et al. 1999; Oquendo MA et al 2014). Interestingly, two major dietary lipid classes, cholesterol and polyunsaturated fatty acids (PUFAs), were significantly associated with higher suicide risk (Pompili M et al 2017; Daray FM et al. 2018). Consistently with the inflammation-related hypothesis of depression and suicidal behavior, C-reactive protein (CRP) blood levels were directly associated with the enhanced risk of attempting and committing suicide (Loas G et al 2016; Dickerson F. et al 2017; Sudol K et al 2017),

suggesting that CRP may be a trait marker of suicidal behavior due to its pro-inflammatory effect together with its growing levels during acute inflammation (Courtet P et al 2015). From a genetic perspective, genome-wide association study (GWAS) identified a region on 2p25 that influences risk for attemptng suicide and contains the ACP1 gene (Willour VL 2012; Pawlak J et al 2016) and polymorphisms in ACP1 which were found to modulate both protection and predisposition to dyslipidemia (Stanford SM et al 2015).

The association between low total cholesterol and cholesterol metabolites serum levels with higher suicide risk has been reported since 1990, when Muldoon and colleagues initially showed that treatments able to reduce cholesterol levels may attenuate the excess of suicidal behaviors and injury deaths in their sample (Muldoon MF et al 1990). These results were confirmed by a large body of literature showing significant associations between altered lipid profiles and higher suicide risk both in patients with specific psychiatric disorders as well as in non-clinical populations (Lee HJ et al 2003; Fiedorowicz JG et al 2007; Chang JC et al, 2013; Aguglia A et al 2017a; Messaoud A 2017; Ayesa-Arriola R et al 2018; Segoviano-Mendoza M et al 2018). Recently, Wu and colleagues conducted a large meta-analysis on 65 epidemiological studies, involving 510.392 participants, and investigated the association between serum lipid levels and 'suicidality' subjects defined as individuals presenting suicidal ideation, suicide attempt, having threatened suicide, or death by suicide. Their findings showed that total cholesterol (TC) and low density lipoprotein cholesterol (LDL-c) levels were lower in suicidal patients than in non-suicidal patients and healthy controls, high density lipoprotein cholesterol (HDL-c) levels were lower in suicidal patients relative to in healthy controls, and triglycerides (TG) levels were lower in suicidal when compared to non-suicidal patients, respectively. Importantly, when the three groups were pooled,

lower serum TC was associated with a 112% higher risk of suicidal behaviors (Wu S. et al 2016).

 Moreover, subjects who attempted suicide within a month from the blood tests had significantly lower TG and higher HDL-c levels than lifetime suicide attempters and those who never attempt suicide, and that TG levels were negatively associated with current suicidal behavior (Baek JH et al 2014). However, other studies investigating a sample of in-patients with type 1 bipolar disorder and other psychiatric conditions failed to confirm these findings reporting no significant differences in lipid profiles between suicidal and non-suicidal subjects (Ahmadpanah M. et al 2015; Bartoli F et al. 2017; Perera S et al 2017).

Recent studies investigated the role of cholesterol levels in violent *vs.* non-violent suicide attempts and showed that the former were significantly associated with lower cholesterol serum levels of approximatively 30% that the latter (Alvarez JC et al 2000; Vevera J et al 2003; Ludwig B et al 2018). Moreover, two post-mortem studies showed significantly lower cholesterol levels in the pre-frontal-cortex (PFC) of violent suicide attempters and significantly higher cholesteryl-ester-hydrolase (LIPA) expression in violent suicide attempters when compared with non-violent suicide attempters (Lalovic A et al 2007; Freemantle E et al 2013).

Given this background, in this study we investigated the differences in CRP, thyroid functioning, TC, HDL-c, LDL-c, and TG serum levels between low-lethality (LLSA) *vs.* high-lethality suicide attempts (HLSA) within twenty-four hours from the suicide attempt and inpatients who never attempted suicide (NAS).

According to this main objective, we tested the following hypothesis: a) lower total cholesterol, HDL-c, LDL-c, and TG serum levels determine HLSA instead of LLSA and NAS; b) CRP levels are higher in HLSA instead of LLSA and NAS.

Materials and methods

Sample

The present study was conducted in a sample of patients who were recruited at the section of Psychiatry of the IRCCS Ospedale Policlinico San Martino - Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, Italy. Participants, potentially considered for study inclusion, were recruited directly from the catchment area of the Psychiatric Clinic of San Martino Hospital among the hospitalized subjects from 1st August 2013 to 31st July 2018.

The inclusion criteria were: a) hospitalization in an emergency psychiatric ward for a suicide attempt; b) aged over 18 years old; c) the willingness to participate in the study by signing a written informed consent. The exclusion criteria were: a) pregnancy or having just given birth; b) having a positive history of acute neurological injury, such as neurodegenerative illnesses, mental retardation, loss of consciousness related to the presence of severe neurological conditions; c) the assumption of lipid-lowering agents; d) the refusal or inability to provide a valid consent prior to participate in the study.

A control group was also included in the sample and it was represented by admitted patients without a history of current and/or lifetime suicide attempts. The control group was matched for age, gender, occupational/marital status, and diagnosis to avoid any bias. We initially screened a sample of 703 patients; however, only 632 subjects voluntary accepted to participate in the study by signing a written informed consent, the remaining individuals were lost due to lack of serum data or because they did not sign the required informed consent.

The study design was reviewed by the local ethics committee.

Assessments and procedures

Socio-demographic and clinical characteristics of recruited patients were investigated during hospitalization through the standardized clinical chart and lifetime computerized medical record, used in Psychiatric Unit. The following patients' domains: age, gender, marital and occupational status, education level, suicide attempts and suicide method were carefully investigated.

All available information have been cross-referred.

Psychiatric diagnoses were evaluated and set according to Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM 5) (American Psychiatric Association 2013). Clinical evaluations have been carried out by expert clinicians and carefully reviewed by a senior psychiatrist (with at least ten years of clinical experience in inpatient clinical setting). If patients had more than one psychiatric diagnoses, the principal psychiatric condition as diagnosed by the treating psychiatrist was recorded. According to previous published studies (Aguglia A et al 2017b; Aguglia A et al 2018), we grouped the diagnosis in four main categories: bipolar and related disorders, depressive disorder, schizophrenia and related disorders, other psychiatric disorders.

Based on Schrijvers and coworkers, we considered suicide as a process, for which suicidal behaviors can be broken down chronologically into "component parts", beginning with the development of suicidal ideation, that progresses to planning, then putting thoughts and plans into action via attempts, and, if successful, culminating in completed suicide (Schrijvers DL et al. 2012).

The term "suicidal lethality" has not yet been defined outside the health literature. Beyond one publication describing suicide lethality as the lethality of the chosen suicide method (Wu YW et al 2009), some theorists like Shneidman and Joiner conceptually identified suicide lethality "as a key ingredient of serious suicidality" (Shneidman ES et al 1996; Joiner T. et al. 2007). We adopted the Joiner's definition of suicide lethality, defined as "the acquired ability to enact lethal self-injury" (Joiner T. et al. 2007). Within suicide lethality, the only individual intent is to perish as a result of the lethality of self-inflicted actions. Methods of suicide attempt were dichotomized in terms of lethality. Therefore, a high-lethality suicide attempt was defined as a suicide attempt that warranted hospitalization for at least 24 h and either treatment in a specialized unit (including intensive care unit, hyperbaric unit, or burn unit), surgery under general anesthesia, or extensive medical treatment (beyond gastric lavage, activated charcoal, or routine neurological observations), including antidotes for drug overdoses, telemetry, or repeated tests or investigations. Conversely, a low-lethality suicide attempt was defined as a suicide attempt that did not meet these criteria (Beautrais AL 2001; Miller M et al 2004; Chen VC et al 2009; Horesh N et al 2012; Huang YC et al 2014; Lee CY et al 2014; Trakhtenbrot R et al 2016; Gvion Y et al 2018).

A routine blood examination was usually performed at hospital admission for all patients as a part of the clinical management routine. Blood samples were taken between 7:00 and 8:30 a.m. after the patients had fasted for at least 10 h and after a psychiatric evaluation; patients who were not fasting were rescheduled. Blood exams included TC, TG, HDL-c, LDL-c, CRP serum levels and TSH Reflex. Blood samples were drawn during the hospitalization in the Psychiatric Clinic and examined in the laboratory analyses of IRCCS Ospedale Policlinico San Martino, Genoa, Italy.

Statistical Analysis

All statistical analyses were performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA) with the value of statistical significance which was set at $p<0.05$.

The socio-demographic and clinical characteristics of the subjects were represented as mean and standard deviation (SD) for continuous variables and as frequency and percentage regarding categorical variables. The Kolmogorov-Smirnov test was conducted to confirm whether all the investigated sample variables followed the normal distribution.

First, the sample was divided in two subgroups according to the presence/absence of current suicide attempts. A statistical comparison between patients with and without current suicide attempts was performed to examine whether there was differences in terms of socio-demographic and diagnostic features. Thus, in order to avoid statistical bias, the two subgroups were matched for age, gender, marital/occupational status, and psychiatric diagnoses.

Subsequently, the subgroup of patients admitted for a current suicide attempt was splitted according to the lethality of the suicide attempts, identifying a subgroup with high-lethality of suicide attempts and a subgroup with low-lethality of suicide attempts. In order to analyze differences between these three subgroups, we used the Pearson $\chi2$ test with Yates correction for the comparison of categorical variables, and ANOVA for continuous variables.

Lastly, a multinomial regression model was performed to detect the variables associated with the lethality of suicide attempt (dependent variable) and each of the other

independent variables previously found associated in the statistical analyses. The probability of entering the equation was set at 0.05.

Results

In our study we recruited a total sample of 632 patients, with a mean age of 49.69±18.97 years. Of the total sample, 478 subjects were females (75.6%) with an educational level of 11.06±3.28 years. 432 subjects were recruited in the case- group and 200 in the control group. There were no statistically significant differences in socio-demographic characteristics (i.e. gender, age, marital status, educational level, working status, and psychiatric diagnoses) between the subgroup of patients who attempted suicide and the subgroup of patients who never attempted suicide (control group). Socio-demographic and clinical characteristics of the included subjects are summarized in Table 1.

Table 1- . Socio-demographic and clinical characteristics in the two subgroups.

	Total sample (N=632)	Suicide Attempt (*N*=432)	No Suicide Attempt (*N*=200)	*t/χ2*	*p*
Gender (female), *N (%)*	478 (75.6)	333 (77.1)	145 (72.5)	1.558	.212
Age (years), *mean±SD*	49.69±18.97	49.13±20.16	50.89±16.11	1.086	.278
Education level, *mean±SD*	11.06±3.28	11.15±3.27	10.86±3.30	-1.046	.296
Marital status, *N (%)* Single Married Divorced Widowed	296 (46.8) 131 (20.7) 147 (23.3) 58 (9.2)	195 (45.1) 93 (21.5) 98 (22.7) 46 (10.6)	101 (50.5) 38 (19.0) 49 (24.5) 12 (6.0)	4.672	.197
Working status, *N (%)*	177 (28.0)	121 (28.0)	56 (28.0)	.000	.998
Diagnosis, *N (%)* Bipolar and related disorders Schizophrenia and related disorders Depressive disorders Others	206 (32.6) 63 (10.0) 202 (32.0) 161 (25.5)	142 (32.9) 37 (8.6) 146 (33.8) 107 (24.8)	64 (32.0) 26 (13.0) 56 (28.0) 54 (27.0)	4.434	.218
Total Cholesterol, *mean±SD*	178.97±42.50	174.14±45.17	189.41±33.86	4.257	**<.001**
LDL Cholesterol, *mean±SD*	117.23±36.47	113.11±37.88	126.15±31.52	4.235	**<.001**
HDL Cholesterol, *mean±SD*	51.55±17.11	52.08±17.39	50.43±16.50	-1.128	.260
Tryglicerides, *mean±SD*	122.63±69.07	114.32±57.38	140.58±86.73	4.514	**<.001**
TSH reflex, *mean±SD*	2.33±1.92	2.30±1.89	2.40±1.99	.629	.529
CRP, *mean±SD*	10.63±23.63	13.52±27.86	4.37±5.61	-4.599	**<.001**

Regarding patients admitted for suicide attempts, 133 individuals (30.8%) committed a high- lethality suicide attempt (HLSA) while 299 subjects (69.2%) carried out a low-lethality suicide attempt (LLSA), respectively. The prevalence of the method used to attempt suicide are showed in Table 2.

Table 2- Type of suicide according to lethality

	Total sample (N=432)
Suicide Attempt, *N (%)*	432 (68.4)
High Lethality	133 (30.8)
Low Lethality	299 (69.2)
Type of Suicide Attempt (N=432) , *N (%)*	
Drug Intoxication	284 (65.7)
Defenestration	40 (9.3)
Drowning	1 (0.2)
Weapon	2 (0.3)
Stabbing	9 (2.1)
Burn/Gas/Caustic	26 (6.0)
Strangling	11 (2.5)
Cuts	59 (13.7)

Considering socio-demographic and clinical features within the three subgroups, the HLSA subgroup was significantly associated to male gender (38.3% *vs.* 16.1% *vs.* 27.5%, p<.001) and diagnosis of bipolar disorder (41.4% *vs.* 29.1% *vs.* 32.0%, p = .007), compared to LLSA and control group, respectively.

When the three subgroups were compared, the HLSA subgroup showed significantly lower total cholesterol levels (151.08±40.90 *vs.* 184.40±43.21 *vs.* 189.41±33.88, p<.001), and LDL-c levels (99.55±33.25 *vs.* 119.15±38.30 *vs.* 126.15±31.52, p<.001) and higher CRP serum levels (24.18±38.69 *vs.* 8.78±19.66 *vs.* 4.37±5.61, p<.001) compared to LLSA and control group, respectively.

Furthermore, the LLSA subgroup showed higher HDL-c levels compared to HLSA subgroup (54.64±16.59 *vs.* 46.31±17.82, p<.001) (no differences between HLSA and control group were observed). Additionally, the control group reported higher

triglycerides level compared to patients admitted for a suicide attempt. No differences in triglycerides levels between HLSA and LLSA were found). Additional differences are showed in table 3.

Table 3- Comparison among three subgroups

	High Lethality (N=133)	Low Lethality (N=299)	Controls (N=200)	F	p	Post-hoc (Bonferroni)
Gender (male), N (%)	51 (38.3)	48 (16.1)	55 (27.5)	26.380	**<.001**	
Age (years), mean±SD	49.62±20.69	48.91±19.95	50.89±16.11	.653	.521	H=L=C
Education level, mean±SD	10.93±3.15	11.24±3.32	10.86±3.30	.963	.382	H=L=C
Marital status, N (%)						
Single	62 (46.6)	133 (44.5)	101 (50.5)		484	
Married	30 (22.6)	63 (21.1)	38 (19.0)			
Divorced	29 (21.8)	69 (23.1)	49 (24.5)			
Widowed	12 (9.0)	34 (11.4)	12 (6.0)			
				5.477		
Working status, N (%)	36 (27.1)	85 (28.4)	56 (28.0) .085		.959	
Diagnosis, N (%)						
Bipolar and related disorders	55 (41.4)	87 (29.1)	64 (32.0)		**.007**	
Schizophrenia and related disorders	16 (12.0)	21 (7.0)	26 (13.0)			
Depressive disorders	41 (30.8)	105 (35.1)	56 (28.0)			
Others	21 (15.8)	86 (28.8)	54 (27.0)			
				17.603		
Total Cholesterol, mean±SD	151.08±40.90	184.40±43.21	189.41±33.88	41.921	**<.001**	L=C>H
LDL Cholesterol, mean±SD	99.55±33.25	119.15±38.30	126.15±31.52		**<.001**	L=C>H

			23.600		
HDL Cholesterol, *mean±SD*	46.31±17.82	54.64±16.59	50.43±16.50	**<.001**	L>H=C
			11.946		
Triglycerides, *mean±SD*	122.13±59.78	110.84±56.03	140.58±86.73	**<.001**	C>H=L
			11.480		
TSH reflex, *mean±SD*	2.04±1.89	2.42±1.88	2.40±1.99	.138	H=L=C
			1.988		
CRP, *mean±SD*	24.18±38.69	8.78±19.66	4.37±5.61	**<.001**	H>L=C
			32.808		

When the multinomial regression was performed, male gender, diagnosis of bipolar disorder, lower total cholesterol level, and higher CRP serum levels predicted HLSA (table 4).

Table 4- Regression analysis

Step	Variables	T	E.S.	Wald	df	p	Exp(B)	95% CI for EXP
Step 1	Gender	-.684	.274	6.250	1	**.012**	.504	.295-.863
Step 2	Diagnosis	.498	.252	3.903	1	**.048**	1.645	1.004-2.695
Step 3	Total Cholesterol	-.022	.006	15.377	1	**<.001**	.979	.968-.989
Step 4	LDL Cholesterol	.004	.006	.479	1	.489	1.004	.992-1.017
Step 5	HDL Cholesterol	-.014	.008	3.483	1	.062	.986	.971-1.001
Step 6	Triglycerides	.004	.002	3.099	1	.078	1.004	1.000-1.008
Step 7	CRP	.017	.005	13.844	1	**<.001**	1.017	1.008-1.026
	Constant	3.388	.759	19.950	1	<.001	.	

Discussion

The present study tested the association between lipid profile, CRP levels, and thyroid functioning in a relatively large sample of psychiatric inpatients who committed HLSA (133 subjects) *vs.* psychiatric inpatients who carried out LLSA (299 subjects) and a control group of psychiatric inpatients who never attempted suicide (200 subjects).

HLSA were more likely to be males and affected by bipolar disorder. This is consistent with previous findings showing that subjects with bipolar disorder presented a higher risk for attempting and committing suicide (Schaffer et al. 2015; Johnston et al. 2017; Rihmer et al. 2018) and supported the higher suicide lethality among males irrespective from their psychiatric diagnosis (Gvion et al. 2018; Rihmer et al 2018; Delpozo-Banos et al 2017; Zalsman et al. 2017).

Our study showed that HLSA was clearly associated with lower total cholesterol and LDL-c, and higher CRP levels when compared with LLSA and controls. To the best of our knowledge, no previous studies investigated the association between suicide lethality and lipid profiles, though our results may be explained in the light of previous evidence showing that violent methods to attempt suicide were associated with lower total cholesterol levels (Alvarez JC et al 2000).

The well-known cholesterol-serotonin hypothesis (Kaplan JR et al 1997) may help to explain these results as lower total cholesterol levels may foster higher central neuroinflammation, thus altering the serotonergic system and leading to higher aggressiveness and impulsivity, especially among males (Tomson-Johanson K et al 2018). In the central nervous system, serotonin plays a role in the suppression of aggressive and harmful behaviors. There are several theories that may explain the potential effect of serum lipid profile (in particular cholesterol levels) on violent conduct and suicide risk. The most blamed mechanism is the reduction of brain serotonin activity which is associated with the risk of attempting suicide. It has been hypothesized that cholesterol levels are associated with the lipid micro viscosity of serotonin receptors and transporters. Since reliable evidence shows that circulating levels of cholesterol – those that may be detected by routine blood tests as those used on the patients in the study –

correlate to the biochemical role of cholesterol as stabilizer of cellular membrane functioning and since membrane cholesterol exchanges freely with cholesterol in the surrounding medium, low membrane cholesterol decreases the number of serotonin receptors through the decreased lipid micro viscosity of the serotonin receptor on the neuronal membrane (Tomson-Johanson K et al 2018: Mann JJ 2013). This process could lead to a poorer suppression of impulsive and violent behaviors, such as suicidal behaviors (Mann JJ 2013). As matter of fact, cholesterol is crucial for membrane stability and neurotransmission that include the alteration of membrane lipid raft structure by the proportions of cholesterol and n-3 PUFAs, affecting the functioning of membrane-bound proteins including serotonin receptors and transporters, and toll-like receptors (Daray FM et al 2018; Allen JA et al 2007). Therefore, low levels of cholesterol might be responsible of increased n-6:n-3 PUFA ratio, thereby promoting neuroinflammation as n-3 PUFAs tend to exert anti-inflammatory properties while n-6 PUFAs levels tend to show a pro-inflammatory activity, and disinhibit, albeit indirectly, two inflammatory intermediates such as nuclear factor kappa-light-chain-enhancer of activated B cells (NFκB) and peroxisome proliferator activated receptors (PPARs), respectively (Liu JJ et al 2015). The abnormal monoaminergic neurotransmission as well as neuroinflammation are two leading mechanisms which are evoked as biological pathways underlying suicidal behavior (Daray FM et al 2018; Sudol K et al. 2017; Allen JA 2007). Lower cholesterol levels are associated with greater impulsivity of suicide attempts and violent methods due to their effects on the serotoninergic system. Indirect evidence suggests an association between attempt lethality and low-cholesterol levels on the basis of the relation between lethality and the choice of violent methods to attempt suicide (Ludwig B et al 2018).

Although, to the best of our knowledge, no study investigated directly the association between CRP, cholesterol, and cholesterol metabolites serum levels and lethality of

suicide attempts, interestingly, a recent study hypothesized a bridge between the well-known cholesterol metabolism process with its associated molecular pathways and the neurobiological underpinnings of suicide risk by showing that the relation between total unesterified cholesterol and suicide risk was significantly mediated by ABCA-1-specific cholesterol efflux capacity (Knowles EEM et al 2018).

Conversely, our results show no differences in total cholesterol and LDL-c levels between LLSA and controls although ANOVA did not confirm these findings. The lack of differences concerning lipid profiles of LLSA and controls could be explained in the light of the lethality of the method used to attempt suicide. For instance, Lalovic and colleagues (Lalovic A et al. 2007) reported no significant differences in cholesterol content between suicide victims and controls in specific brain regions such as the frontal cortex, amygdala, or hippocampus. However, when suicides were classified as violent or non-violent according to the used method, violent suicides were found to have lower grey-matter cholesterol content in the frontal cortex compared to non-violent suicides. Other authors (Pompili M et al 2010), albeit in a small sample, reported no difference in the levels of total cholesterol and triglycerides among attempters and non-attempters.

Our findings show that TG were significantly higher in the control group than in LLSA and HLSA subgroups, among which no significant differences were reported. This is consistent with previous studies showing lower TG levels among suicide attempters when compared with controls without a positive history of suicide attempts (Chang JC et al 2013; Ayesa-Arriola R et al 2018; Segoviano-Mendoza M et al 2018; Wu S et al 2016). Lower TG levels were reported in subjects who attempted suicide in the month before the survey compared with subjects who had suicidal ideation in the month before the survey and never suicidal controls (Baek JH et al 2014).

Moreover, our findings do not show any differences regarding TG levels in LLSA and HLSA subgroups; to date, no previous study investigated the possible association between the lethality of suicide attempts and TG levels. There are studies in the current literature that reported no differences in TG levels in violent *vs.* non-violent suicide attempts, though they did not consider the lethality of suicide attempts (Bartoli F et al. 2017; Da Graça Cantarelli M et al 2015).

Our study should be considered in the light of the following limitations; first, this is a cross-sectional study, and we cannot assess whether a decrease in TC or TG may have caused a mood episode with active suicidal ideation leading to suicide attempts or if the presence of a mood episode originated a loss of appetite and a consequent loss of weight altering lipid profiles. Thus, given the main nature of this study, we could not evaluate the direct causal relation between suicidal behaviors and lipid profile. Moreover, our results could not be adjusted for the psychopharmacological medications that both cases and controls were taking when assessed and this may have influenced our findings. However, subjects taking lipid-lowering agents were not included in the sample. Third, a detailed medical history, including careful information about the body mass index (BMI) were not available. Neither blood pressure nor glycaemic values were collected and, consequently, included in the analysis. However, we only included those subjects with stable clinical conditions apart from what was related to suicide attempts.

Conclusions

Our data suggest that low total cholesterol serum levels may increase the risk of highly lethal suicide attempts and low triglycerides serum levels increase suicide risk – as well

as low TC levels do – but do not influence the lethality of the attempts. To the best of our knowledge, no previous study has investigated TC and TG levels in respect to the lethality of suicide attempts. Therefore, further studies should focus on this association in order to confirm these preliminary results and shed light on the complex neurobiological mechanisms underlying suicidal behaviors.

3. Suicide lethality & Seasons and photoperiod a case-control investigation

Introduction

Suicide and all related behaviors are a serious social and health problem worldwide. The World Health Organization (WHO) reported that approximately 800.000 people died by suicide worldwide in 2016, and that the number of people attempting suicide each year is even higher. Suicide was the second leading cause of death among 15-29 year old people in 2016 with an annual global age-standardized suicide rate of 10.5 per 100.000 population (WHO, 2017).

The etiology and risk factors related to suicidal behaviors are complex and not yet fully known. Several studies underline how suicide results from the combination of psycho-social, biological, cultural, and environmental factors (Christodoulou et al., 2012; Rumble et al., 2018). Psychosocial factors include life event stressors such as family violence, sexual or substances abuse, parental separation, loneliness and hopelessness, traumatic life events, social isolation or discrimination among sub-populations (Bando et al., 2017; WHO, 2017; Ásgeirsdóttir et al., 2018; Lee et al., 2018; O'Neill et al., 2018; Veisani et al., 2018). Moreover, different biological risk factors for suicidal behaviors have been identified, such as mental illnesses (in particular bipolar disorder and borderline personality disorder), involuntary admissions, altered of metabolic

parameters, increased inflammatory markers, cyclothymic temperament, altered neurotransmission involving serotonin and dopamine dysfunctions (Hawton and van Heeringen, 2009; Costa et al., 2015; DeShong et al., 2015; Aguglia et al., 2016; Pompili et al., 2017; Serafini et al., 2017; Batty et al., 2018; Daray et al., 2018; Fond et al., 2018; Kuo et al., 2018; Peng et al., 2018).

However, suicidal behaviors are not completely explained by the complex network of these phenomena and epidemiological studies have been carried out in order to shed further light on these dynamics. For instance, the study of geographical variations in suicide rates suggested additional explanatory variables (Sun et al., 2011; Woo et al., 2012) and significant associations between seasonality and both completed and suicide attempts have been reported (Hakko et al., 1998; Ajdacic-Gross et al., 2010; Christodoulou et al., 2012; White et al., 2015; Aguglia et al., 2016; Canner et al., 2016; Akkaya-Kalayci et al., 2017; Sawa et al., 2017; Dixon and Kalkstein, 2018; Hofstra et al., 2018; Rumble et al., 2018). In particular, Coimbra and colleagues (2016) confirmed the significant role of seasonality on suicide attempts and Galvao and colleagues (2018) showed that completed suicides occurred more frequently in spring and early summer in their survey on 2.146.418 completed suicides. However, mechanisms underlying the seasonality of suicidal behaviors are still unclear and need further investigation.

Therefore, recent studies focused on the possible role of other environmental factors involved in suicidal behaviors such as air pollution, photoperiod, daylight exposure and meteorological variables, with controversial results (Donagay et al., 2003; Toro et al., 2009; White et al., 2015; Makris et al., 2016; Akkaya-Kalayci 2017; Casas et al., 2017; Jee et al., 2017; Min and Min, 2017; Seregi et al., 2017; Dixon and Kalkstein, 2018; Gao et al., 2019). Interestingly, Fountoulakis et al. (2016) carried out a vast study in

twenty-nine European countries about the relationship of male and female standardized suicidal rates and economic and climate variables. The Authors reported that the climatic effect (cold climate) was stronger than the economic one in increasing suicide rates and showed that in Europe suicidality followed the climate/temperature cline which was from south to north-east.

Furthermore, several clinical studies indicated that suicide rate is also correlated to increased ambient temperature (Doganay et al., 2003; Toro et al., 2009; Likhvar et al., 2011; Grjibovski et al., 2013; Helama et al., 2013; Holopainen et al., 2014; Qi et al., 2014; Akkaya-Kalayci et al., 2017; Bando et al., 2017; Carleton, 2017; Dixon and Kalkstein, 2018; Gao et al., 2019). In fact, studies on the association between temperature and suicide showed that 26.6%-60% of variation in suicides could be explained by temperature variations (Helama et al., 2013; Ishii et al., 2013; Fountoulakis et al., 2016), but not with sunlight exposure especially for completed suicide (Gao et al., 2019).

Moreover, evidence showed significant associations between hours of sunshine and completed suicide carried out through violent methods (Linkowski et al., 1992; Maes et al., 1993; Preti and Miotto, 1998; Wu et al., 2009; Vyssoki et al., 2012; Vyssoki et al., 2014; Ludwig and Dwivedi, 2018). These studies confirmed the hypothesis of higher lethality of suicidal behaviors during spring/summer, higher daylight exposure or associated with increased ambient temperature. However, few studies investigated the ~~possible~~ relationship between seasonality and lethality of the suicidal attempts. Lin et al. (2008) showed that violent suicides are more likely to be influenced by seasonal factors, with significant peaks in March-May (early to late spring), than non-violent suicides. These findings were not confirmed by Veisani and colleagues (2017) who

reported seasonal trends in spring and autumn of suicides by violent methods and in spring and summer for what concerns non- violent suicides.

However, to the best of our knowledge, the possible influence of photoperiod and seasonality on the lethality of suicide attempts has not been investigated yet. Therefore, in this study we investigate (a) the potential role of seasonality on the lethality of suicide attempts in psychiatric in-patients; (b) the potential role of the photoperiod on highly lethal suicide attempts (cases) compared with low-lethality suicide attempts (controls) in a sample of psychiatric in-patients.

Materials and methods

2.1 Sample

Subjects were recruited at the Section of Psychiatry, Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI), IRCCS Ospedale Policlinico San Martino, University of Genoa (Italy). Participants were recruited in our inpatient service from 1st August 2013 to 31st July 2018. Subjects were considered for the study if their psychopathological conditions were deemed clinically stable as assessed by the two senior researchers, GS and MA.

Silverman's operative definition of "suicide attempt" has been used in this study, i.e. a kind of suicide- related behavior, classified as a suicidal act and characterized by self-inflicted, potentially injurious behavior with non- fatal outcome for which there is evidence – either explicit or implicit - of intent to die (Silverman et al., 2007). Moreover, our definition involves the presence of lethal intent that can be of varying intensity but has to be present in the decision to carry out the suicidal act (Pompili et al., 2015).

Inclusion criteria were: a) hospitalization in our emergency psychiatric ward for suicide attempt; b) aged more than 18 years old; c) acceptance to participate in the study by

signing a written informed consent after the aims of the study and study procedures were explained thoroughly. Exclusion criteria were: a) pregnancy or having just given birth; b) having a positive history of acute neurological injury, such as neurodegenerative illnesses, mental retardation, loss of consciousness related to the presence of severe neurological conditions; c) the refusal or inability to provide a valid consent prior to participate in the study.

The study design was conducted in accordance with the guidelines provided in the current version of the Declaration of Helsinki. The study design was reviewed and approved by the local ethics committee.

2.2 Assessments and procedures

Psychiatric diagnoses were formulated according to Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) (American Psychiatric Association 2013) and the subjects were divided into four diagnostic groups: schizophrenia-related disorders (referred to hereinafter as schizophrenia), bipolar and related disorders, depressive disorders and others (included personality disorders and substance-related disorders) according to previous studies (Aguglia et al., 2017; Aguglia et al., 2018). Clinical evaluations were carried out by expert clinicians and were carefully reviewed by a senior psychiatrist (with more than ten years of clinical experience in inpatient clinical setting). If patients had more than one diagnosis, the principal diagnosis was recorded.

Socio-demographic and clinical aspects of the subjects were investigated through the standardized clinical chart and lifetime computerized medical record used in our Psychiatric Unit. Age, gender, marital and occupational status, education level, previous suicide attempts, suicide method were recorded. All available information have been

cross-referred. Furthermore, we considered month and season upon admittance in the psychiatric ward (i.e., Autumn from 21st September to 20th December, Winter from 21st December to 20th March, Spring from 21st March to 20th June, Summer from 21st of June to 20th September). Hospitalization period was divided according to the sunlight exposure in spring-summer (s-s) (highest solar intensity period) and autumn-winter (a-w) (lowest solar intensity period), according to existing literature (Aguglia et al., 2017; Aguglia et al., 2018), defining "photoperiod" as the number of hours of day light and is able to influence the individual's physiology and metabolic cycles.

In the wake of Schrijvers et al. (2012)'s conceptualization, we considered suicide as the final step of a multilayered process starting with suicidal ideation that progresses into planning and continues with the enacting of suicidal thoughts and plans by attempting suicide that may end up in completed suicides.

In the present study, we used Shneidman's and Joiner's definition of lethality and divided our sample of suicide attempts into two groups according to the level of lethality:

(a) "high lethal suicide attempt" (HLSA) for attempts that needed hospitalization for at least 24 hours and either treatment in a specialized unit (including intensive care unit, hyperbaric unit, or burn unit), surgery under general anesthesia, or extensive medical treatment (beyond gastric lavage, activated charcoal, or routine neurological observations), including antidotes for drug overdoses, telemetry, or repeated tests or investigations;

(b) "low lethality suicide attempts" (LLSA) that are attempts that did not meet these criteria (Beautrais, 2001; Miller et al., 2004; Chen et al., 2009; Horesh et al., 2012;

Huang et al., 2014; Lee et al., 2014; Trakhtenbrot et al., 2016; Gvion and Levi-Belz, 2018).

HLSA (cases) were compared with LLSA (controls) in the second part of our analysis in order to evaluate the differences between these groups better.

2.3 Statistical Analysis

Socio-demographic and clinical data were considered as mean and standard deviation (SD) for continuous variables and frequency and percentage regarding categorical variables. Kolmogorov-Smirnov test was used to confirm that the investigated variables had a normal distribution.

In order to analyze differences between cases and controls (HLSA vs LLSA), we used the Pearson χ^2 test with Yates correction for the comparison of categorical variables, and the t-test for independent samples for continuous variables. Comparative analyses on number of admissions were adjusted for age and gender. Furthermore, bivariate analyses were conducted.

All statistical analyses were performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA) with the value of statistical significance set at $p<0.05$.

Results

Four hundred forty-seven (N=447) subjects meeting our inclusion criteria were hospitalized after a suicide attempt in the study time-frame. Eleven subjects refused to take part in the survey and four subjects were not admitted to the psychiatric unit because of major physical comorbidities, e.g. cancers and advanced sarcoidosis.

A final sample of 432 subjects was formed, mean age 49.1 (±20.2) years old. 77.1% of the sample were females, 45.2% were single (of which 32% divorced and 68% never married), and 28% were employed at the time of enrollment [Table 1]. 32.9% of the sample had bipolar disorder, 8.6% schizophrenia and 33.8% major depressive disorder [Table 1].

Table 1: socio-demographic and clinical characteristics of the sample included.

	Suicide Attempt (*N*=432)
Gender (female), *N (%)*	333 (77.1)
Age (years), *mean±SD*	49.1±20.2
Education level, *mean±SD*	11.2±3.3
Marital status, *N (%)*	
Single	195 (45.2)
Married	93 (21.5)
Divorced	98 (22.7)
Widowed	46 (10.6)
Working status, *N (%)* Yes	121 (28.0)
Diagnosis, *N (%)*	
Bipolar and related disorders	142 (32.9)
Schizophrenia and related disorders	37 (8.6)
Depressive disorders	146 (33.8)
Others	107 (24.8)
Type of Suicide Attempt , *N (%)*	
Drug Intoxication	284 (65.7)
Defenestration	40 (9.3)
Drowning	1 (0.2)
Weapon	2 (0.3)
Stabbing	9 (2.1)
Burn/Gas/Caustic	26 (6.0)
Strangling	11 (2.5)
Cuts	59 (13.7)
Lethality of Suicide Attempts	
High lethality	133 (30.8)
Low lethality	299 (69.2)
Lifetime suicide attempts, *mean±SD*	1.2±1.1

Month of admissions, N (%)	
January	26 (6.0)
February	30 (6.9)
March	37 (8.6)
April	38 (8.8)
May	49 (11.3)
June	42 (9.7)
July	36 (8.3)
August	40 (9.3)
September	29 (6.7)
October	29 (6.7)
November	40 (9.3)
December	36 (8.3)
Seasonality, N (%)	
Autumn	101 (23.4)
Winter	88 (20.4)
Spring	131 (30.3)
Summer	112 (25.9)
Photoperiod, N (%)	
Spring-Summer	243 (56.2)
Autumn-Winter	189 (43.8)

One hundred thirty-three (N=133, 30.8%) of the sample committed a HLSA and two hundred ninety nine (N=299, 69.2%) was in the LLSA group. The HLSA group peaked in the months with a higher sunlight exposure [Figure 1].

Figure 1: differences in terms of month admissions between high vs low lethality suicide attempts
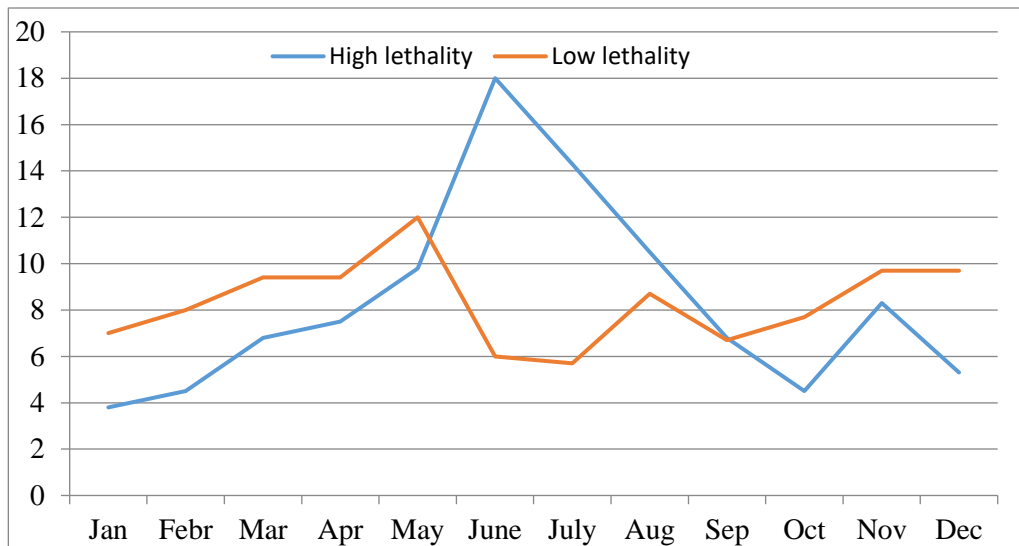
$\chi 2 = 30.726$; df = 11; **p = .001**

Major differences between HLSA and LLSA were reported in June (18.0% vs 6.0% respectively) and July (14.3% vs 5.7% respectively) [Table 2].

Table 2: seasonality and photoperiod differences between high vs low lethality suicide attempts

	High Lethality (N=133)	Low Lethality (N=299)	t/χ2	df	p
Seasonality, N (%)					
Spring	48 (36.1)	83 (27.8)	19.516	3	**<.001**
Summer	47 (35.3)	65 (21.7)			
Autumn	23 (17.3)	78 (26.1)			
Winter	15 (11.3)	73 (24.4)			
Autumn, N (%)	23 (17.3)	78 (26.1)	3.974	1	**.046**
Winter, N (%)	15 (11.3)	73 (24.4)	9.793	1	**.002**

Spring, N (%)	48 (36.1)	83 (27.8)	3.024	1	.082
Summer, N (%)	47 (35.3)	65 (21.7)	8.865	1	**.003**
Photoperiod, *N(%)*					
Spring-Summer	95 (71.4)	148 (49.5)	17.990	1	**<.001**
Autumn-Winter	38 (28.6)	151 (50.5)			

Bivariate correlation analysis between seasonality/photoperiod in the whole sample and HLSA were positively associated with summer (r=.143; p=.003) and during highest solar intensity period (r=.204; p<.001). Moreover, HLSA was negatively associated with autumn (r=-.096; p=.046) and winter (r=-.151; p=.002) [Table 3].

Table 3: Correlations between high lethality suicide attempts and environmental variables

	Lethality of Suicide Attempt
Autumn Winter Spring Summer Longer photoperiod	-.096 (p=.046) -151 (p=.002) .084 (p=.082) .143 (p=.003) .204 (p<.001)

Discussion

Our study shows that suicide attempts carried out in summer, when there is the highest

solar intensity were more likely to be highly lethal compared with those carried out in other times of the year. June and July were the months in which highly lethal suicide attempts peaked when compared with low-lethality suicide attempts. Moreover, suicide attempts carried out in autumn were less likely to be highly lethal than in other photoperiods and seasons. Our sample showed a prevalence of major affective disorders and this may partly explain the particular trend in the lethality of suicide attempts that we reported because of the complex influence of daylight, circadian rhythms and seasons on affective disorders and suicide attempts. This is consistent with previous studies reporting more season- and circadian- related fluctuations of suicide rates among patients with mood disorders, in comparison to those with schizophrenia (Valtonen et al., 2006).

Our findings confirm previous evidence showing that suicidal behaviors exhibit both circadian (van Houwelingen and Beersma, 2001; van Houwelingen et al., 2010) and seasonal rhythms (Germain and Kupfer, 2008). Both in attempted (Valtonen et al., 2006) and completed suicides (van Houwelingen and Beersma, 2001) time patterns were detected. In particular, our findings are consistent with previous evidence that reported the highest rate of completed suicides between May and July when the period of daylight is always shorter for the a.m. hours than it is for the p.m. hours and this influences mechanisms that decode the duration of the melatonin signal in the melatonin-target tissues. Thus, increased sunlight exposure causes alterations in the metabolism of melatonin and serotonin (Brewerton et al., 2018, Maruani et al., 2018).

The reaction of the organism both to the stimulation of a longer period of light (as in spring and summer), and to the exposure of higher temperatures, may be implicated in the destabilization of the psychopathological framework, potentially favoring the

increased rate of high lethality suicides detected. Regarding light effects, prolonged light exposure could dysregulate circadian rhythm causing sleep disruption. It is known that light exposure is the primary signal for the central clock in the suprachiasmatic nuclei (SCN) of the hypothalamus and suppresses melatonin synthesis by the pineal gland. The SCN influences the circadian rhythm of body temperature, as a key synchronizer of clocks in peripheral tissues (Potter et al., 2016; Maruani et al., 2018). The hypothalamus is anatomically connected with the thalamus and the limbic cortex, constituting a functional framework that links bodily sensations to emotional responses. In humans, the limbic cortex is in turn associated with the anterior portion of the insular cortex, processing convergent sensory information to produce an emotive correlation. Besides, areas of the insular cortex that are activated during recall of feelings are also activated during the conscious sensation of pain and temperature (Kandel et al., 2013). It is possible to hypothesize, therefore, a link between the perception of significant heat (from high temperatures) and an emotional correlation of discomfort, which can translate into behavioral anomalies in subjects at risk. Furthermore, patients with mood disorders are especially vulnerable to circadian dysregulation and sleep disruption, with an increased risk to the onset of mixed states (Muneer, 2017) and consequently to present dyscontrol of impulses and suicidal behaviors.

The photoperiod spring-summer, in which we reported the highest lethality in suicide attempts, is a particular time of the year from the circadian-clock point of view because of the challenge to alignment of the circadian rhythms with the sleep-wake cycle.

Interestingly, in-depth findings about the brain activity during this photoperiod are provided by studies on animals that showed how the very long day might challenge the network within the circadian pacemaker that is comprised of the evening and morning

active cells, and that takes part in the seasonal adaptation in diurnal animals such as sheep and horses (Lincoln et al., 2003; Hazlerigg et al., 2004). When day lengths become shorter in fall and winter, the morning active cells dominate the circadian output, e.g. the sleep-wake behavior. However, this dominance is gradually transferred to the evening active cells as the days get longer in spring and the coincidence effect of the morning and evening active cells disappear when the melatonin signal duration becomes insufficient to sensitize adenylate cyclase and to support a peak expression of the morning-active cells (Nagoshi et al., 2010). The speeding up of the evening active cells (e.g. by sunshine) makes the morning active cells higher firing rate in spring-summer photoperiod but not in fall-winter and this determines important melatonin-dependent effects on clock- gene expression in spring and fall among which CRY2 and PER2 genetic variants have been reported. The expression of CRY2 and PER2 variants is regulated by the circadian pacemaker system also in human and have been associated with vulnerability for unipolar and bipolar depression (Lavebratt et al., 2010). Different clock- genes have been associated with higher suicide risk in bipolar patients such as such as CLOCK gene that is associated with violent suicide attempts, thus possibly involving the lethality of the attempts: TIMELESS, PER3 and ARNTL gene that are involved in the modulation of the course of bipolar illness, e.g. the recurrence and frequency of episodes which have a predictive value for suicide attempts (Pawlak et al., 2017).

Moreover, lower melatonin levels have been significantly associated with completed suicides in post- mortem studies (Kurtulus Dereli et al., 2018) and this may further support our findings of more lethal suicide attempts and lower levels of melatonin in spring – summer when there are less hours of darkness during which melatonin is produced in pinealocytes. Interestingly, melatonin results from the n- acetylatylation of

5-HT via the catalyzation of enzymes aralkylamine n-acetyltransferase (AANAT) and acetylserotonin O-methyltransferase (ASMT) that are regulated by clock- genes. Therefore, decrease in 5-HT and increase in daylight impair melatonin synthesis (Tosini et al., 2012; Meng et al., 2018).

However, different hypotheses have been developed to shed light on the relationship between suicides and spring-summer photoperiod and one of these explains how the increase in temperatures experienced by the human body in spring and early summer would contribute to cerebral hyperactivity associated with symptoms such as anxiety that increase the risk of suicide (Vaughan et al., 2011; Helama et al., 2013; Holopainen et al., 2014; Gao et al., 2019). Moreover, classic theories about the association between 5-HT dysfunctions and suicidal behaviors have been developed to explain the seasonal pattern of suicides worldwide. In particular, disruption in the functioning of the 5-HT system link affective disorders, anxiety, seasonal admissions with mania and violence and/or impulsive behaviors like sexual abuse, aggression, homicide and obviously suicide (Marazziti et al., 2013; White et al., 2015; Brewerton et al., 2018).

Recently, the use of blue light hotspots in railway platforms to decrease the incidence of railway suicides has been investigated and contrasting evidence has been reported (Matsubayashi et al., 2013; Matsubayashi et al., 2014; Ichikawa et al., 2014). For instance, Matsubayashi et al. (2013) indicated that suicide deaths decreased significantly by 84% across the eleven Japanese stations where blue lights were installed. However, Matsubayashi et al. (2014) reported that the suicide numbers were reduced significantly by 74% at the stations with blue lights installed without systematically increasing at nearby platforms without blue lights. Interestingly, Ichikawa et al. (2014) further tested

the previous findings by Matsubayashi et al. (2013, 2014) and argued that blue lights may have much more limited potential as a suicide prevention strategy than previously suggested, as suicide attempts occurring when platform lights are installed and turned on only comprise a small number of the total rail-related attempts. However, current understandings of this existing, albeit small, effect of blue light hotspots on impulsivity and suicidal behaviors suggest that the stimulation of melanopsin retinal ganglion cells by blue light activates the retino-hypothalamic tract to the SCN that act melatonin pathways. In particular, evidence showed that blue light in the range of 460–480 nm is more effective compared to monochromatic light of 555 nm in phase-shifting the human circadian clock, thus leading to decrease in heartbeat rates and promoting relaxation (Tosini et al., 2016).

Future research should focus on effective prevention strategies targeting the use of light dependent neuronal pathways to decrease suicide attempts and suicide rates. In particular, the use of blue light hotspots and melatonin oral supplementation programs in subjects with mood disorders during photoperiods at higher suicide risk should be further investigated.

4.1 Limitations

The present study should be considered in the light of the following limitations. First, patients' seasonal environment and psychological factors as well as the presence of acute life-events fostering the suicidal crisis have not been investigated. Second, our findings result only from one city and we could not evaluate the possible confounding effect of weather, humidity and other geographical variables co-existing with the photoperiod. Diagnosis were formulated by expert clinicians according to the DSM-5 but no structured interviews have been performed. The lethality of suicide attempts has

been measured through clinical parameters, but no rating scale was used to evaluate it. No data concerning the photoperiod in which previous suicide attempts were carried out have been collected. Moreover, data concerning pharmacological compliance together with possible autonomous decisions to suspend pharmacological treatment in spring-summer in patients with mood disorders were not collected. Therefore, we cannot evaluate the possible effect of autonomous pharmacological suspension in spring-summer on suicide attempts.

Conclusions

Despite the large body of evidence, further studies are needed to provide deeper understandings on the delicate molecular network that links suicide behaviors, seasonality and daylight in order to be able to develop more effective prevention and treatment strategies in the future. Future research may lead to the development of specific medication targeting these molecular systems that may help both suicide prevention and recurrence of acute affective episodes.

RESEARCH AREA C

PSYCHODYNAMIC

UNDERSTANDINGS

OF

SUICIDAL BEHAVIOURS

Borderline suicidal patients: destructiveness and its communicative potential

The clinical encounter with borderline patients is a complex challenge for therapists. Confrontation with intense dynamics call into question the limits of the psychotherapeutic method as well as the therapist's capacity to contain and symbolize powerful destructive behavior, which sometimes seem impossible to tame.

Borderline patients are eager to restore a state of complete fusion with the object, but are also terrified of emotional dependency. Thus, they swing "between periods of exposure and periods of restriction; they are exposed to intense anxiety from their objects when the defensive organization fails, and suffer restricted, though tolerable, object relations when it is again established" (O'Shaughnessy, 1981, p. 359).

These relational vicissitudes often express deep failures which occurred during the period of the original holding environment. The painful experience of not being able to find primal objects "exactly where the infant created" them (Winnicott, 1953) – because they are depressed, narcissistically fragile, or drowned in painful secrets – reoccurs over and over during the treatment of these patients. To a certain extent borderline patients begin treatment because they unconsciously seek an object capable of not just putting their emotions into words, but also of being able to give shape and meaning to the violent melancholic anxieties which lie untransformed at the *core* of their being, so that they are inevitably forced to live on the brink of the depressive position and unable to work it through. Borderline structures differ substantially from classic neurotic ones. Because the Ego cannot transform and symbolize intense feelings of helplessness and non-existence experienced in early infancy, such feelings remain in the mind as unrepresented nuclei, deep in the self, and cannot be expressed verbally. Rather, these raw proto-emotions are likely to be re-actualized in the therapeutic relationship through

non-verbal communications, such as body-centered sensations, like movements and postures but also tone of voice and rhythm of speech. Thus, therapists have to take account of the non verbal aspects of communication and carry out a thorough working through process of their countertransference emotions and sensations in which unsymbolized feelings emerge and seek transformation.

In this study, we investigate and address how traces of these painful experiences tend to emerge in an extremely destructive way within the transference relationship. Through a detailed presentation of the different emotional dynamics aroused in the therapist's countertransference, the complexity of the patient's defensive organization could be accessed, while many of its nuances had be received, tolerated, contained, and transformed in order to allow the patient, Miss K., to make contact with her profoundly melancholic nucleus.

This research belongs to the context of "research *in* psychoanalysis" (Widlocher, 2003) since no conclusive evidence is provided as to how to deal with and transform acute destructive behavior during treatment. Our aim is to show in detail what takes place in the transference relationship during destructive enactments and offer hypotheses and suggestions to stimulate further understanding and research. To this end, we present three sessions, describing the therapist's step-by-step countertransference reactions. We investigate and discuss the communicative value of destructive behavior and the existence of life forces lying beyond what looks like a death instinct in defused form.

Clinical material

Drawing on the case of a 25-year-old woman, Miss K., we present and explore the high communicative potential of the intense and violent countertransference experiences that often transpire while treating patients with conflicts on a narcissistic-identity level. We

present three subsequent sessions which occurred midway in the fourth year of Miss K.'s three-time per week psychotherapy on the couch. In particular, we try to show what took place and emerged in moments of acute destructive behavior in the transference-countertransference relationship and how therapists receive, contain and work through – to the best they can – painful and barely tolerable emotions to help patients carry out the first symbolization process without enacting their destructiveness. Therefore, we do not expound our clinical material as a claim to show what should be done when working with violent dynamics. We simply present examples of the complex countertransference emotions which arise when therapists are confronted with acute destructive behavior and hatred. In addition, we show how the elaboration of the working through process fosters the emergence of the severe melancholic object that lies deep within the Self.

Miss K. came to me [Paola Solano] in a severe state of confusion and rage because yet another boyfriend had left her. She had been suffering violent panic attacks, outbursts of rage and peaks of anxiety during which she was unable to study or leave her house. Indeed, because of these episodes she had stopped going to university some months previously. Miss K. lived alone with two cats in a flat close to her older brother's while her younger brother still lived in their parents' home in a town two-hours away from Genoa. The first time I met Miss K, she told me of the pain she felt when she discovered that her boyfriend had been dating another girl for almost a year while Miss. K. was still living with him. She told me that she had attempted suicide at age sixteen because of the embarrassment, isolation, and shame she experience from being bullied at school. Henceforth, relationships with her peers had been characterized by high competitiveness, anger, suspicion and fear of rejection. During that particular session, Miss K. looked distant and detached and I wondered whether she realized what she was telling me. After the suicide attempt, Miss K. had a period in which she often went

clubbing and drank heavily "in order to get rid of the shame, rage and pain". For some time she became promiscuous and "lost her mind" until she finished high school and began university. Miss K. was a talented student, governed by a harsh superego, which required her to not accept anything but the highest marks in school, which resulted in her being two years behind in her studies. During her first years at university, Miss K. developed mild anorexic symptoms and vaginismus that impaired her sexual life for a few years.

Miss K.'s parents were well-educated, aloof people who had difficulty relating to their only daughter and preferred their boys. Miss K. described her mother as an absent-minded, unkempt, intellectual woman who had fallen into deep depression when Miss K. was two years old. Miss K. believed the depression was caused by a late miscarriage because she had found some old medical records from that period. However, Miss. K. had never felt close enough to her mother to ask about it.

Indeed, Miss K. told me that she felt rejected and neglected by her. Miss K.'s mother had never looked after her but left her father in charge of her upbringing and education. The father, a businessman who was often abroad for work, had no time for Miss K.'s emotional needs and she felt that he had always preferred her brothers to her. Her parents had no knowledge of Miss K.'s suicide attempt nor her distress because she had asked her older brother to hide it from them, which he did. She explained, "I had to deal with it because it was my problem and not theirs". When Miss K. moved to Genoa to attend university, she didn't accept any money from her parents but paid for her studies and upkeep by working very hard in a restaurant. She neither spoke of her hobbies or her lively, though superficial, social life to her parents or in treatment because, "you, my therapist, aren't here to listen to nice things and, besides, they are largely outnumbered by sad things to the point that the nicities have become meaningless to me". It wasn't

until midway through her second year of treatment that Miss K. briefly mentioned her love of climbing. Up to that point, the only image that came to mind of Miss K.'s daily life appeared as an empty, grey space studded with outbursts of rage and sadness in which nothing alive could exist.

Miss K. had no previous psychotherapeutic treatments and had never taken any psychopharmacological medication.

Monday Session

Miss K. arrived ten minutes early and rang the doorbell twice quite vigorously, which was something she had never done. When I opened the door, she rushed into the waiting room without looking at me or shaking my hand. She was carrying a tennis racket and dropped it heavily on a chair in the waiting room. She looked tense and angry. On entering the consulting room, she said that she had left the racket in the waiting room because there was no point bringing it in. The loud, sharp ringing of the doorbell and the noise of the tennis racket hitting the chair in the waiting room still resonated in my head like violent chimes, leaving little room for anything else. Miss K. lay on the couch and said, "Will you be here for our sessions this week? If not we can change our session times so I don't miss any!" I wondered why she had asked that because there had been no cancellations during the previous month, nor were there any approaching holidays. I told her that she looked worried as though something imminent would cause her to miss a session, stealing our time together. She nodded and said that her cousin had told her that her ex- boyfriend was getting married at the end of the summer. She paused and then began shouting, "You don't understand! Our work here is useless because even if I do get better that won't help me find a husband! I'm just wasting my time here! I'm becoming more and more selective and this won't help me find a husband!" She

continued that she couldn't be happy for someone else's happiness and I should agree with her that our work was just making her sicker and sicker instead of helping her. She told me this in a grave, threatening voice and I felt the urge to agree with her. I perceived Miss K.'s pressure as an attack on my mind which initiated an inner struggle between my agreeing with her and feeling her thoughts intruding on mine, while trying to keep to my own ideas created an endless battle with her. I decided to tell her that she was very sad about her ex-boyfriend's wedding and that she probably felt under pressure to feel and think how others expected her to feel which profoundly contrasted with her actual feelings. This pressure had become so strong in her mind that she has to constantly fight it just to survive and not be intruded upon and annihilated. Miss K answered me angrily, "What do *they* want to impose on me?" The atmosphere was becoming more and more tense, and after a while, I told her that maybe she felt she was expected to be happy for someone else's happiness but she just couldn't. During the session, she had wanted me to agree with her that her growing awareness of herself was destructive and that our work was useless. After a pause, I told her that this was a very violent mechanism relentlessly ticking over in her mind in such a way that revealed that nothing could work and left her feeling more and more miserable and resentful every time. Miss K. answered in a low, serious voice "I'm not envious of him! I just think that our work won't help me get married. I can be the most self- aware person in the world, but that won't help me. That is the truth. Our work is useless and I feel sicker and sicker all the time! These four years of treatment have been useless! I've had five different boyfriends but they all left me. We haven't done anything here!" I felt angry and frustrated. In fact, I really felt like shouting something back, but managed to stay quiet and continued listening. "Tell me - what kind of improvements do you see? Tell me! Tell me!" she shouted, followed by total silence, which provoked an extremely tense atmosphere making me feel I had been sent to sit in the corner. After a few minutes, I found myself

attempting to list her improvements in my mind but as soon as they emerged I discarded them as if "they weren't good enough" to be put forward. I felt helpless and the thought of having nothing to give her became more and more insistent. A sense of paralysis began to spread around the room and I felt increasingly forced to agree with her. I felt I was engaged in a struggle where either her opinion or mine could survive and be violently imposed onto the other's mind. I told her that there was a lot of

tension between us as if we had to impose our own ideas into the other's mind because no agreement was possible. After a short pause, I suggested that apparently we could only be on opposite banks of the river even though she was afraid of being abandoned because, otherwise, she would feel too threatened and, therefore, had to make sure she got her whole week of sessions. "No. I don't think that your way of working is the right way to help me! You're making me more and more sick and I'm losing everything I have! I can't stand anybody now! If we continue like this I'll have to take medication because our work here just makes me sicker! I'll have to take medication because I can't bear this anymore! I told you this a few months ago, but you didn't give me anything and now I'm getting worse!" she responded quickly. I felt accused of not listening to her, of belittling her sufferings and also of purposely denying her medication. I replied, "You are in a lot of pain and want me to understand how desperate you are. You're afraid you won't be able to stand this anymore and will have to take medication to cope with it, which is something we can think about should you feel you can't bear this any longer and need some relief". After several minutes of silence, she continued that a few days ago she had planned to go to the cinema with a friend but after she got there and bought the tickets he didn't show up. "He left me standing in front of the cinema holding our tickets without even contacting me! When I called him, he said that his girlfriend was jealous and would not let him come. He didn't tell me because he was afraid that she would have got mad if he had texted me". Miss K. said that she knew her friend's

girlfriend was envious of their friendship because she knew that it would last longer than their relationship and that was what made her so angry. Miss K. continued that a friend of hers had invited her to study together for their next exam. She had adamantly rejected her suggestion because this girl had let her down twice when she wanted to go shopping with her some weeks before. "My friend said that I'm wrong and I misunderstand her but she doesn't listen to me and doesn't see my

point of view," Miss K. shouted. Then, an increasing sense of sadness gradually began to dominate the session. I imagined the sad image of Miss K. standing alone in front of the cinema holding the two tickets and waiting for her friend, full of expectations, although he never arrived. Sadness together with a painful sense of disillusion filled my mind and these feelings almost made me cry. I could feel tears swelling up, then suddenly wiped away by Miss K.'s harsh words about the undeniable evidence that she was right about her friend and about me. "When I started to come here I was full of expectations that now barely exist. I'm deeply disappointed in your work!" she added sharply. All contact with sadness, guilt, and sorrow was quickly denied and replaced by violent reproaches. I felt disappointed and put down as if the opportunity to make contact with more depressive feelings had suddenly vanished. I said that I was very disappointing for her because she felt that I kept failing her. I added that during the session we had both become, by turns, the Miss K. who was left standing in front of the cinema, holding two tickets, waiting for a friend who never came because envy had prevented any contact. I realized that my words were imbued with sadness, but I still felt some hope of making contact with her. Miss K. stiffened on the couch and shouted, "I don't know what you're talking about! I'm fed up speaking about these things! I'm not going to do that anymore!" The session was nearly finished. I said that she had come to the session bringing her hope of spending a nice evening with a good friend along with the sadness of the disappointment in being rejected and left alone holding the two

tickets. I added that the contact with sadness was too painful for her to bear and she had to wipe it away with anger to attack our capacity to work together. Miss K. said coldly, "That's the point. Now that you got there what difference does it make? You tell me! My whole life I've been standing holding two tickets that I couldn't use! What are you going to do about it? You tell me! So what? Now that you know!" Then she remained silent for the last few minutes of the session. When I told her it was time to stop she jumped off the couch, grabbed her bag, books and tennis racket and left the consulting room banging the front door violently as she went out.

I was tense and the noise of the banging door resonated inside me. I felt threatened by an intense, impending fear of being abandoned that gradually became a feeling of helplessness. Interestingly, I began to notice that the threatening fear of being abandoned was connected to the idea of being so disappointing to her in such a way that she got fed up and couldn't stand it anymore. I was afraid of being too disappointing and too much of a burden for her. Gradually, anger surfaced and I began to feel that she was a heavy burden for me because whatever I proposed would fail and I was helpless. I wondered about my capacity for helping her and whether I was really doing the best possible for her. I felt that my professional identity was deeply challenged and put at stake by these complex emotions. Suddenly, I realized that maybe Miss K.'s fear of missing her sessions, which she had spoken of at the beginning of the session, had to do with these feelings and her fear of being turned down because of her capacity to perceive what she was doing to the object. I felt unsure whether Miss K. would come to the next session but a sense of sadness towards her helped me re-establish contact with a sense of continuity.

Some notes on the Monday Session

Miss K. presented complex mental structures in which different levels of psychic functioning co-exist and switch rapidly during sessions. Before putting forward our reflections on the clinical material, we would like to underline that our aim is to simply present some general suggestions on how Miss K.'s material can be understood and worked through without laying claim to any conclusive answers on either theoretical or technical issues. Rather, we have attempted to present the clinical material in the most precise way possible in order to provide a detailed account of this kind of experience and develop their own thoughts about therapeutic encounters with patients like Miss K. in moments of acute destructive behavior.

The beginning of the Monday session was enigmatic and unsettling. Miss K. made a noisy entrance as if to mark her return intensely, starting with continuously ringing the consulting room doorbell then throwing her racket onto the consulting room chairs with a clatter. However, by doing this she made it evident that she was leaving one of her belongings i.e. a part of her, namely her racket, outside the consulting room. She said that there was no sense bringing it in and went on to speak about recuperating some sessions that the therapist was oblivious to.

Although no justification of this initial behavior came about in the dynamics that followed, nor did Miss K. broach the subject of what had been left in the waiting room, it communicates her claustro-agoraphobic dilemma (Rey, 1994) from the very beginning. Did she leave her capacity to play behind? Was it something too aggressive that had to be left outside in order to protect the therapist? Why was Miss K. afraid of the therapist's absence and wanted to make sure that she would be able to recuperate the missed sessions?

Miss K. appeared to be caught between her need to get close and merge with the object

in order to prevent abandonment and persecutory fears of being overwhelmed and swallowed by it. Thus, she sank into a state of despair in the absence of the object or when perceived as separate, hence, hindering any psychic creativity. However, at the same time, any contact with the object was also threatening and intrusive, stimulating violent destructive behavior which severed both inter- and intra-psychic links.

Miss K.'s experience of living in a reduced dimension results from her attacking emotional links and the linking function *per se* (Bion, 1959) that can be recognized in the therapist's countertransference as being isolated in a state in which her mind is filled with "loud and acute noises that leave little room for anything else". For instance, the commotion Miss K. made on her arrival could be considered as a "free associative activity" (Authors, 2015) splitting links through non verbal communicative modes i.e. destructive behavior. Consequently, the therapist's mind was immersed in an auditory dimension that represented Miss K. cutting off parts of herself to be left "outside" the session like the tennis racket that remained in the waiting room. Miss K. had to resort to non verbal communicative modes both at the beginning and end of the session, when she slammed the door leaving the consulting room, to handle and express the fears stirred up by the encounter and the separation from her therapist caused by her claustro-agoraphobic anxieties. Moreover, the recurrent countertransference experience of intrusion as something "imposed" or "forced" into the therapist's mind together with not being able to come to an agreement further display Miss K.'s fear of separation from the object which becomes a desire to penetrate it and fuse with it, restoring a primal unity "that could be so intense as to surpass human understanding" (Rey, 1979, pp. 202).

The therapist's attempt to put Miss K.'s anxieties into words and the cutting off mechanisms that were enacted both physically and through the auditory dimension produced a short moment of emotional contact. Miss K. spoke of a couple that was

getting married. The groom was her ex-boyfriend; sorrow and sadness surfaced because she was unable to emotionally engage in a stable relationship in her daily life or in her therapeutic treatment. However, the brief contact with these emotions were intolerable and triggered Miss K's destructive rage. She was unable to accept anything helpful from the therapist whose suggestion was taken as a threat since it challenged her omnipotence. Miss K. could not acknowledge the existence of anything different from her and so her predicament became intolerable. Meanwhile, the therapist's mind was swamped with violent projective identification that attempted to annihilate not only her capacity of thinking but also any difference between her and the object. The aim of Miss K's hostility was to oppose any separation between herself and the object which reminds us of Green's theory about the need for the container to adjust completely to the patient's requirements in order to be acceptable while working with borderline patients (Green, 1996).

At the start of the session the therapist was immediately confronted with different, complex technical issues. The role and function of interpretation in the face of excessive tension towards indifferentiation in Miss K.'s situation enhanced the emergence of the regressive forces at play in the transference from the beginning of the session. Should the therapist put Miss K.'s emotions into words? Would it help in decreasing her anxiety or stir up feelings of intrusion and threaten Miss K.'s fragile boundaries? How could Miss K. begin to build the emotional links (Freud, 1920) that allow the tapering of death drives and foster symbolization?

Drawing on her countertransference, the therapist worked on the process level to try to interpret the violence of the emotions displayed together with the impossibility of making contact with Miss K. The touching image of Miss K. and the therapist on "opposite banks of the river" portrays not only the difficulties of being together within

the therapeutic couple but also Miss K.'s inner split which leaves her with profound feelings of loneliness. This image made Miss K. even angrier and respond that the treatment was "making her sicker and sicker" and she was afraid she would need medication for her deteriorating condition. In this way, Miss K. expressed her fear of dependency on the therapist and the treatment, and the risk of making contact with split, violent proto-emotions that frightened her so much. Indeed, the fact that Miss K. felt worse is a significant development to some extent because she became more aware of her feelings and emotions although this made her feel threatened and furious at the same time. Nevertheless, the therapist's comment, in an attempt to contain her anxieties, did not touch this aspect. Perhaps Miss K.'s anger could have been due to her fear of changing, "becoming more and more selective" and developing her own capacity for thinking which produced the dreadful thought that the treatment could have an uncontrollable influence over her, like medication. Midway into the session, Miss K.'s envious rage was not only directed to the therapist's thinking capacity but also to her own perceiving-self which was annihilated (Segal, 1993). This caused her to shout, "Tell me! What kind of improvements do you see? Tell me! Tell me!". The continuous attacks to Miss K.'s perceiving-self led to a growing sense of arrogance and stupidity throughout the session (Bion, 1958). Consequently, Miss K. became progressively identified with a phallic, omnipotent, superior object that attempted to engage the therapist in a sado-machistic struggle that tended to structure an enclave because of the powerful splitting forces at play (O'Shaughnessy, 1992). Miss K.'s therapist could perceive the patient's attempts at engaging her in a struggle that would isolate the therapeutic couple in a split off enclave and experienced some of these dynamics in her countertransference. For instance, the therapist found herself attempting to list the patient's improvements in her mind but as soon as they emerged she discarded them as if "they weren't good enough" to be put forward. Powerful splitting and fragmenting

forces were at work and the therapist could only feel helpless and the thought that she had nothing to give Miss K. became more and more consistent in her mind. A sense of paralysis began to spread around the room and the therapist felt increasingly forced to agree with her opinion. Hence, the therapist's restricted capacity of thinking was a result of her being partly caught in Miss K.'s entrapment which was also present at Miss K.'s intrapsychic level.

In patients like Miss K., once the object has become significant for the patient every small fault of the object is a source of severe disappointment and is experienced as intolerable abandonment (Winnicott, 1954). Obviously, the therapist cannot fulfill these expectations and becomes a disappointment; her presence is in fact limited by the setting and cannot always be available for Miss K. The intensity of disappointment in the therapist's countertransference shows us not only the strength of idealization, i.e. expectations, and devaluation in Miss K.'s inner world but gives us some hints about Miss K.'s early environment and the primal encounter with her environmental mother. Miss K.'s primal object appears far away, detached and barely accessible for her in the transference thus generating strong feelings of devaluation and narcissistic emptiness (Winnicott 1971; Green, 1993) from which Miss K. shielded herself through violent and uncontrolled bursts of destructive behavior. The result is that all emotional links are severed and Miss K. is plunged into a desperate state of emptiness which tends to re-produce the original narcissistic wound through repetition compulsion in their turn. To some extent, the dynamics in which Miss K. kept on bringing her damaged object to the sessions together with continuous, envious dismantling e.g. the friend who left her sad and disappointed waiting for him at the cinema, is "that which the patient brings to analysis" (Rey, 1988).

Tuesday Session

I was wondering whether she would have come or not when Miss K. arrived on time as usual. "Please come in," I said, opening the door, and Miss K. replied quickly, "Thanks". She looked tense. Her eyes were so dull they seemed to be covered by an opaque film. She glanced at me hurriedly and lay on the couch. In the silence that followed I felt the atmosphere becoming more and more tense and threatening. Then she said in a solemn voice, "I don't know what to tell you first. I felt humiliated and belittled by yesterday's session. I was talking about trust, about me placing my trust in our work here, when you shifted the focus by talking about taking medication when you should have known that I'm terrified of depending on something or someone and would never, ever agree to taking it! This makes me think that you haven't understood anything about me and you even talked about my travelling as a way of running away from reality when travelling is something I've always done!" I felt confused because I knew I hadn't said that during the last session and I also knew it was too dangerous to tell her. While I sensed not to challenge the reality she was bringing into the session, I also perceived a growing sensation of being imprisoned mixed with craziness spreading around the room. I asked her, " Did we talk about your travels yesterday?" and Miss K. replied vehemently, "Yes!! You said that I need to run away to America and Russia without realizing that these are two very different things! I'd like to go and live in the USA, where I have an aunt, in order to start over again while I just went to Russia on holiday! I'd like to continue my studies in the USA but you don't understand this!" I felt angry and tense as though something was about to explode any minute. Gradually, my anger decreased and I made contact with a sense of belittlement, humiliation and injustice that I felt unable to fight. There was no room for any evidence that contrasted Miss K.'s predicament and I could only accept it and take in her thoughts.

I began to feel unsure about what had taken place in the previous session as if I couldn't recollect clearly what had happened: everything seemed so confused. I felt ashamed and

guilty as if I wasn't paying sufficient attention to her to the extent that I had become the disappointing object she was so angry with. After a few minutes of silence I suggested that maybe I had mentioned Rome in the previous session. Miss K. had been lying motionless on the couch but responded by shouting, "No! You spoke about the US too!" and began weeping. Then, she said resentfully that we were not doing anything right and she had never felt understood by me during our work together. Her tone was scornful yet triumphant at the same time which was not only irritating but also humiliating as if all our progress meant nothing to her at that moment. Miss K.'s rebuff made me feel betrayed and worthless; the threat of being abandoned gradually came forward in my mind.

After a long pause, I told Miss K. that something was happening between us and we should discuss it. I commenced, "Yesterday, and even more today, I'm disappointing you. It looks as if I'm even more of a disappointment in your mind than what I really am because you ascribed things to me that took place in your inner world which never really happened. You bring your pain into the session and tell me how wrong I am for you and how unhappy you are with me. Then, to make me understand how much you are suffering, you refer to topics that didn't come up yesterday". Miss K. shouted, "They didn't come up yesterday because other things did! Yes, it's true the US didn't come up yesterday!!... Listen, I came here today despite having a fever. OK?!" I felt deeply touched by her admission and perceived that she was calling on my capacity for human understanding and surrendering to the strain that had been gradually developing between us. I waited a while before saying that I wasn't against her and we were looking at what was happening to see how we could use it. Then, I continued that she was right and that she was showing me how much she was frightened of depending on something but more importantly on someone. Regardless, Miss K. persisted as though I hadn't spoken at all and said, "All right! We didn't mention the US, but you spoke about medication! You

did! We shouldn't have spoken about it but you changed our focus!" I tentatively suggested, "It's true, I did speak about medication. Maybe I wasn't right to do so, but can we talk about why I did it?" Miss K. said, "You did it because you didn't understand what I said! You thought it was a good idea to mend my anguish with something that could provide quick relief! I continue to suffer and I don't understand why. Why am I continuing to suffer? Why?" I felt helpless and defeated because I couldn't reach Miss K. who kept on repeating the same question in such a way that excluded any progress we had achieved.

An expanding impression of dreariness came forward together with the feeling that what we had just experienced had been isolated leaving me alone with it and unable to share it with Miss K. Next, I suggested that I was very disappointing for her because she felt that I didn't understand her. I added that even though she came to our session despite having a temperature she kept on following a destructive train of thought. There was a lull before I continued, "I think you know how much you're frightened of depending on someone. You were scared when you realized how much you care about our work because of your fear of being abandoned. It is as though you were dealing with a disappointing internal mother that you can't help looking for and desiring but whom you attack fiercely out of fear and rage as soon as you make contact with her". Miss K. remained silent for several minutes and I felt I had managed to make contact with her. She was very still on the couch but then started biting her nails and took off a bracelet she was wearing. "You always tell me the same things! I've been listening to these things for years and there is still no progress!" she said swiftly.

Miss K. kept on saying that our work was useless and nothing could help her. Every time I made a suggestion to illustrate what was happening, Miss K. attacked it and our work more intensely. I felt increasingly angry and annoyed by her repetitive dismantling

process which made me look forward to the end of the session while a subtle sense of threat and fear crept in. I began to feel that I had failed her and was unable to help her. I started thinking that I was useless and had nothing to give her and her only remaining choice was to go elsewhere be helped properly because I was unintentionally wasting her time. Shame and guilt engulfed me for being such a disappointment and unable to fulfill my commitment. I felt stuck in a dimension where time stood still but my feelings were extremely vivid. These feelings were like a sort of undeniable and ultimate truth with no possibility of development or transformation. However, I slowly began to notice that the more Miss K. continued to dismantle and fragment our work in a dull, monotonous voice the more I felt her despair growing and imbuing the session alongside a sense of immobility in a hopeless, fault-finding dimension. Gradually, my anger and sense of helplessness and paralysis became a sensation like a heavy burden on my chest that turned into a sense of turmoil. I wondered if Miss K. realized what she was doing and felt lonely. So, I told her that I was sorry she suffered so much and that I understood how distressing it was to live with these maddening emotions that seemed to nullify all chances of help and cancel everything else. Miss K. remained silent and began to cry. Then, just before the end of the session, she said, "I don't see any progress…". After Miss K. left, I felt that I had done everything I could to help her, and wondered how she would deal with these awful feelings until the following session. I was left with a slight sense of apprehension.

Some notes on the Tuesday Session

The beginning of the session shows us how borderline patients like Miss K. threaten and oppose the therapist and the analytic technique by pushing them to the limits of the symbolization processes. Miss K. was unable to rely on words as a sufficiently effective

mode of communication. As soon as Miss K. managed to say that she had felt "belittled and humiliated" in the previous session she moved rapidly forward and projected these emotions into her therapist in a sort of reversal mechanism from passive to active.

This may have been the first attempt towards subjective appropriation of experience together with a desperate way of communicating her torment to the therapist through unconscious-to-unconscious communication. Moreover, the therapist's feelings of confusion and turmoil generated by Miss K. twisting her comments about medication and the reality of the previous session may help us understand how patients like Miss K. experience certain interpretations. In fact, being able to receive an interpretation in the inner world is determined by the subject's capacity to tolerate passivity derived from a "good enough" encounter with the primal object. When this cannot take place, passivity is replaced by "passivation" (Green, 1999) and the object's words become persecutory and intrusive in the sense that they are experienced as attempts to strip the subject's words of their meaning. Thereby, content is distorted and the fragile boundaries of the patient's identity are challenged.

On another level, the "growing sense of craziness and imprisonment" felt by the therapist may echo Miss K.'s fear of becoming mad which she had spoken about in the previous session. Although Miss K.'s associations communicate deep feelings of estrangement and detachment they also express the patient's wish (and need?) to keep contact with the therapist albeit through perversion. In particular, Miss K.'s powerful intrusion into the therapist's mind and attempt to appropriate her thoughts through perversion could show a strong desire to become fused together, thus denying any separateness or envy.

Furthermore, this session clearly demonstrates Miss K.'s intense "effort to drive the other person crazy" (Searles, 1959). The patient's early experience of an unpredictable,

unreachable object is re-activated in the transference and she has to continuously check whether it can "hold her in her mind", i.e. remember her previous sessions. In this sense, Miss K. covets an object that differs deeply from her because of her need to evacuate whatever comes from the outside and tries to confer meaning to her experiences. Hence, the therapist's attempt to show her what had really happened in the previous session made Miss K. even angrier and increased the strength of her projections. The therapist felt trapped in a dimension in which "there was no room for any evidence that contrasted Miss K.'s predicament" and had an almost delusional quality of "absolute, ultimate truth" that reminds us of the delusion of the clarity of insight (Meltzer, 1976).

The therapist's comment highlighting that she had been made even more disappointing in the patient's mind than what she really was underlines how Miss K. was keeping the object in a damaged state that prevented any transformation. She did this by attributing things to the therapist that actually took place in her inner world and never really happened. Notably, Miss K. made the therapist appear more and more damaged in the transference which may express her increasingly desperate attempts to bring about concrete reparation of her damaged inner objects. However, true reparation is never achieved thereby her inner objects remain increasingly damaged and inner destructive cycles are reinforced so much so that the patient's mind is unable to get rid of them.

To some extent, this is what Miss K. actually expects from the treatment: psychic reparation of her objects, hence, reinstated as good objects without which life cannot be normal, satisfying and worth living (Rey, 1988). However, the second part of the therapist's suggestion, "certain things that took place in Miss K.'s inner world never really happened" had complex meanings and emotional resonances. If, on the one hand, the therapist's intervention is aimed at restoring Miss K.'s contact with her emotional reality, on the other, it risked hindering the patient's regression process by addressing

her "adult part" (Balint, 1968) too directly. Although it is important to tame the strength of certain emotions, that otherwise risk dangerous escalation, we believe that the suffering part of the patient's Self may have felt rejected and misunderstood by this comment. In part, this sequence portrays the therapist's defensive attempt to re-establish the hierarchy which was threatened by madness when confronted with Miss K.'s destructiveness.

Did this sado-masochistic scenario serve Miss K. as a way of approaching the object, albeit driven by hatred, and dragging the therapist out of her neutrality? Could we consider this struggle as Miss K. desperately striving to grab hold of and be kept in the detached, depressed primal object's mind?

Miss K.'s forlorn cry, "Listen to me! I came here today despite my fever. OK?!" communicates her tremendous effort to make contact with an unreachable, emotionally untouchable inner object that cannot remove her pain in a magical way, ergo, "I'm still suffering!" The object can offer nothing but words while Miss K.'s infantile self would almost need to be physically held like a newborn baby. In this sense, although the therapist's comment about the disappointing inner mother is correct, it is somehow premature and may be experienced as the therapist trying to temporarily shift the focus from Miss K.'s aggression to restore her third position (Ogden, 2004) in the treatment. Subsequently, Miss K.'s difficulty in introjecting this interpretation may be due to her primitive mental functioning in which the therapist *did not represent* the mother, rather the therapist *was* the mother (Winnicott,1954). Thus, Miss K. could understand the therapist's interpretation cognitively, but not feel nor make use of it emotionally because she was functioning at a more premature level.

Despite complications evolving during the session, the therapist's capacity of containing painful countertransferencial feelings of uselessness and inadequacy that later became

anxiety and loneliness enabled the therapeutic couple to make contact with early traumatic feelings that Miss K. had experienced in the relationship with her environmental mother. We believe that the unfolding procedure of the therapist working through her countertransference gave Miss K. "an interpretative experience" (Authors, 2016), i.e. the experience of a reliable and stable container which allowed and fostered a silent working through process that "verbal interpretations" had failed to provide her with.

Thursday Session

Miss K. arrived a few minutes late and upon arrival shook my hand with a half-smile on her face. When she lay on the couch, she told me that she was sorry for what had happened during the Tuesday session and she was also aware that certain topics had not been touched on Monday. However, she felt that she was unable to agree with me at that time because it would have been like giving in to me in a moment of frustration and anger. I felt relieved and moved by her words. There was silence, then Miss K. continued that she disagreed with me about identifying me as her disappointing mother because "everybody was disappointing" for her now and she didn't think she was identifying the whole world with her. I told her that it was important that she could tell me how sorry she was for what had happened and that she could speak about it in the session. Miss K. stiffened on the couch and said in a sarcastic voice, "Do you think that I was right to get so mad for no reason? I told you off although I knew very well that I was wrong!" Miss K. was ruthless to herself. I felt that I had to protect her capacity to feel genuinely sorry for what had happened during the previous session and from the harshness that she now directed towards herself. So, I tentatively said that she probably wanted to make me experience how painful it is for her to be with a person who disappoints her. I added that she showed me how her anger made the person even more disappointing by attributing imaginary shortcomings to reinforce her belief. After a pause, Miss K. said, "I think I'm

the only disappointing person here. What you described often happens when I'm with my friends too. They usually leave me afterwards. They just run away! No one understands me!" Her voice was slowly changing and I felt an escalating tension spreading through the room. She continued, "I can't discuss it. I have no points in my favor so I'm constantly striving to make everybody understand that I'm suffering. I'm not getting any better and I don't know how I can make it any clearer! I'm getting tired of repeating this and nobody is getting the message!".

In a certain way, she sounded detached as if she was chanting an eerie sort of lullaby which contrasted the content of her words. I started to feel bored and had to strain to keep contact with what she was telling me. I said, "I'm exhausting you because I'm not listening nor understand so you need to tell me again and again. It is as if your words cannot reach me." "No!" she replied, "I'm wearing myself out because I'm not getting any better and then I move the focus onto you to take a break. I've always disappointed myself and everybody. This has nothing to do with you!" I suggested, "You take it for granted that you're disappointing me." Miss K. remained in silence and then shook herself briefly. In a sarcastic voice she said, "I can't be so cool if nobody wants to spend time with me. I'm always alone!" A threatening atmosphere started to pervade the room and I knew that I had to be very careful of what I said. I felt under pressure to agree with her and that what she had just said was the only sensible thing to say or think. I told her that she sensed she was wrong and that maybe sometimes she had to blame others for being disappointing because otherwise the feeling of being wrong would have choked her. Miss K. took my comment as an accusation and answered me angrily that she was disappointed with certain people at the moment, but it was not always like that. She continued, "I've been telling you that I feel like a disappointment for almost four years now so there's nothing new about that! I'm very sick now…" I said, "I can see that." This was followed by silence, then I asked her if I had made her angry by speaking.

Miss K. started crying and said, "No, not when you talk like this".

Then, I told Miss K. that she was telling me how much she cared for me and felt sorry about getting angry with me. I added that I felt she was very frightened of "touching" me too much emotionally in case I couldn't stand her anymore and she wanted to protect me in some way. This was followed by a very long silence that I perceived as thoughtful at the beginning but soon became a void. At that point I said that maybe it was difficult to discuss what I had said. Miss K. answered that she thought that it was very late and not much work had been done because there had been no significant changes. She said she was exhausted and didn't feel like going to the beach, meeting people, sitting the upcoming exams or even playing with her cats or meeting her brothers. "I feel that life is too burdensome for me. I don't have a problem anymore because I've become the problem itself!" she said quietly. I felt that Miss K. was somehow detaching herself from what was going on in the session which began to seem abstract and emotionally meaningless. I felt worried about these dynamics that I perceived to be draining our work and preventing her from keeping contact with it. So I said that it was true she was suffering a lot and I felt sorry for her. Miss K. made an incomprehensible sound at this as if it had reached her. I continued that by working on these delicate matters together we were also working on what made her suffer so much in her daily life. Miss K. remained silent and said that she wasn't interested in what I was saying because she was in pain. She added that she didn't understand what I was talking about and that we weren't working on anything in particular. She was simply getting sicker and sicker! I felt angry and disarmed and told her that it was difficult for her at that moment to not cancel out what I had just said. Miss K. said that she was beginning to dread loneliness and this was unacceptable. I said that maybe it was because she wiped all her feelings and emotions away and wondered how anybody could remain with her in this condition. Miss K. replied that she had never thought about suicide. She had attempted it without

really thinking about it but she believed she had no reason to live. "I'm too much for everybody," she said. "I can barely cope with myself so how can I expect other people to do so? You're only here because it's your job. That's why!" The session was about to end and I told her that maybe, if she really felt that I wasn't interested in her, she wouldn't have brought all these feelings into the treatment. To this, Miss K. answered in tears that our work was her last hope.

[On Friday, Miss K. rang me asking whether we could have an extra session the following week. I told her that we were going through a very difficult period and we could talk about it on Monday and arrange it].

Some notes on the Thursday Session

The silent containment provided by the therapist's working through process of her countertransference allowed Miss K. to realize and communicate her sorrow and concern for having severely damaged the object through her anger at the beginning of the session. Miss K. was able to recognize and acknowledge her fury and frustration and became partly aware of the sado-masochistic dynamics that had taken place during the previous sessions which she described as, " giving in to the therapist".

However, contact with these emotions along with the growing sense of intimacy soon became unbearable for Miss K. She had to regain a "safe" distance between her and the therapist; hence, "everybody was disappointing". Miss K. was frightened that if she accepted and experienced the therapist as the maternal object, she would become too relevant and less controllable in her inner world.

When the therapist tried to re-establish contact with Miss K.'s sorrow by telling her that it was important that she could say how sorry she was for what had happened and speak about it, the patient re-evoked her unconscious fear of becoming mad (Green, 1996).

This is illustrated by Miss K. stiffening on the couch and saying in a sarcastic voice, "Do you think that I was right to get so mad for no reason? I told you off although I knew very well that I was wrong!" Miss K.'s violence towards herself and her statements of being "*the only* disappointing person here" and "getting mad for *no reason*" may express her fear of going mad and identifying herself with a critical, self-reproachful Superego. Despite the touching significance of these words, the therapist felt that Miss K. had spoken them in a detached way, thus, using them more to sever the affective link between them than to make contact with her narcissistic sufferings. Perhaps the sense of boredom which gradually came over the therapist was brought about by the intensity of the projective phenomena; Miss K. had used her destructive energy to make the therapist distance herself so Miss K. could triumphantly accuse her of having abandoned her patient. In this way, Miss K. avoided making contact with her depression.

After the first phase of the session, which was characterized by paranoid-schizoid mechanisms, Miss K. verbalized her feelings of being "very sick" and the therapist answered that she could "see that". This mutative moment in which the therapist's comment allowed Miss K. to experience a sort of mirroring (addressing the visual dimension suggested by "I see you / I see your pain") let the patient feel that her deep torment was accepted and received. Then, Miss K. said in a genuine voice that the therapist's words didn't make her angry, "when she talked like this". Miss K.'s malignant regression (Balint, 1959) briefly gave space to a true sense of being held by the object while making deeper contact with herself.

The end of the session was particularly touching and reveals the reason why patients like Miss K. use powerful defenses to avoid the encounter with the other and the profounder parts of themselves. Deep inside their (true) Self lies a dreadful, frightening melancholic nucleus that harbors painful feelings, such as the useless and senselessness

of their lives and the belief that nobody could be sincerely interested in them. "I don't have a problem anymore! I've become the problem itself!" declared Miss K., identifying herself with the lost, damaged object that is continuously attacked by a highly persecutory Superego (O'Shaughnessy, 1986). These kind of dynamics allowed Miss K. to become aware of her fear of loneliness, or rather, to be alone with these dreadful emotions. The therapist's capacity of understanding the depth of the narcissistic abyss that lies beyond Miss K.'s destructive anger and grievances (Feldman, 2008) is fundamental in finding the best balance between silence and interpretation; moments in which the Ego needs to be supported to foster a decrease in splitting and so making contact with painful emotions. Notably, premature contact with distressing areas of the Self may put the patient's life at risk. However, at the same time, avoidance of regressive movements may lead to interminable analysis that take place in the "*as if*" dimension in which the true Self never emerges from the defensive organization.

Conclusion

In this study, we have presented and discussed both the difficulties and communicative potential of bodily countertransference during destructive enactments in the treatment of severe borderline patients. Through Miss K.'s material and the analysis of the therapist's countertransference, we have shown and investigated different aspects and nuances of the defensive organization structured around a melancholic nucleus embedded deep in the Self of borderline patients. The exacting working through process of the intense transference dynamics, which mainly took place through non verbal communicative modes, allowed the gradual emergence of Miss K.'s melancholic nucleus together with the story of her unrepresented, early traumatic experiences during the initial encounter with the object. Future research should further investigate the role and communicative potential of destructive enactments as an opportunity for original traumatic experiences to emerge and be transformed in treatment together with technical

issues in order to receive, contain and transform these powerful dynamics.

4. General concluding remarks

The most innovative aspect of this research is the integrated approach for the assessment and treatment of suicide risk analyzed through different special populations and aspects. In particular, the presented historical perspective supports and confirms current understandings about the need for a multi-disciplinary approach to the study of suicidal behaviors aiming to the implementation of a modus operandi that has in the development of effective clinical tools its major objective.

Biological, clinical and therapeutic understandings of suicidal phenomena should be further investigated in order to develop effective prevention strategies both at population and individual level involving different professional approaches and perspective because every effort should be made to help those who suffer and protect and preserve human life fostering its quality.

5. REFERENCES

Addington, J., Williams, J., Young, J., Addington, D. Suicidal behaviour in early psychosis. Acta Psych. Scand., 2004; 109(2): 116-20.

Aghanwa, H. S. The characteristics of suicide attempters admitted to the main general hospital in Fiji Islands. J. Psychosom. Res., 2000; 49: 439- 445.

Aguglia A, Albert U, Maina G. Serum lipids and lifetime suicide attempts in patients with obsessive-compulsive disorder. J Obsessive Compuls Relat Disord. (2017a) 15:1-6.

Aguglia A, Borsotti A, Cuniberti F, Serafini G, Amore M, Maina G. The influence of sunlight exposure on hospitalization in emergency psychiatry. Chronobiol Int. (2017b) 34:1413-22. https://doi:10.1080/07420528.2017.1374286.

Aguglia A, Borsotti A, Maina G. Bipolar disorders: is there an influence of seasonality or photoperiod? Rev Bras Psiquiatr. (2018) 40:6-11. https://doi:10.1590/1516-4446-2016-2144.

Aguglia, A., Moncalvo, M., Solia, F., Maina, G., 2016. Involuntary admissions in Italy: the impact of seasonality. Int. J. Psychiatry. Clin. Pract. 20(4), 232-238. http://doi:10.1080/13651501.2016.1214736

Ahmadpanah M, Haghighi M, Jahangard L, Borzoei S, Heshmati S, Bajoghli H, et al. No evidence for metabolic syndrome and lipid profile differences in patients suffering from bipolar I disorder with and without suicide attempts. Int J Psych Clin Pract. (2015) 19(3):168-73. https://doi:10.3109/13651501.2015.1049277.

Ajdacic-Gross, V., Bopp, M., Ring, M., Gutzwiller, F., Rossler, W., 2010. Seasonality in suicide – A review and search of new concepts for explaining the heterogeneous phenomena. Soc. Sci. Med. 71, 657-666. http://doi:10.1016/j.socscimed.2010.05.030.

Akiskal, H.S., Akiskal, K.K., Haykal R.F., Manning J.S., Connor P.D., 2005. TEMPS-A: progress towards validation of a self-rated clinical version of the Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego Autoquestionnaire. J. Affect. Disord. 85, 3-16.

Akkaya-Kalayci, T., Vyssoki, B., Winkler, D., Willeit, W., Kapusta, N.D., Dorffner, G., Özlü-Erkilic, Z., 2017. The effect of seasonal changes and climatic factors on suicide attempts of young people BMC. Psychiatry. 17, 365. http://doi:10.1186/s12888-017-1532-7.

Alem, A., Kebede, D., Jacobsson, L., Kullgren, G. Suicide attempts among adults in Butajira, Ethiopia. Acta Psych. Scand., 1999; 397: 70-6.

Al-Gamal, E., Alzayyat, A., Ahmad, M.M., 2016. Prevalence of internet addiction and its association with psychological distress and coping strategies among university students in Jordan. Perspect. Psychiatr. Care. 52(1), 49-61.

Alvarez A. (2002). *The savage god: A study of suicide*. Bloomsbury Publishing: New York

Alvarez JC, Cremniter D, Gluck N, Quintin P, Leboyer M, Berlin I, et al. Low serum cholesterol in violent but not in non-violent suicide attempters. Psychiatry Res. (2000) 95:103-8.

Ambrus, L., Sunnqvist, C., Asp, M., Westling, S., Westrin, Å., 2017. Coping and suicide risk in high risk psychiatric patients. J. Ment. Health. [Epub ahead of print]

American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th. Arlington (VA): American Psychiatric Publishing (2013).

Anderson, A., Lester, D., Rogers, J.R., 2008. A Psychometric Investigation of The Suicide Opinion Questionnaire. Death. Stud. 32, 924-936.

Anderson, P. L., Tiro, J. A., Price, A. W., Bender, M. A., Kaslow, N. J. Additive impact of childhood emotional, physical, and sexual abuse on suicide attempts among low-income African American women. Suicide Life Threat. Behav., 2002; 32(2): 131–138.

Andres A R. (2005). Income inequality, unemployment, and suicide: a panel data analysis of 15 European countries. *Applied Economics*, 37(4), 439-451.

Angst, J., Clayton, P.J. Personality, smoking and suicide: a prospective study. J. Affect.Disord.,1998; 51: 55–62.

Aquinas T. (2006). *Summa Theologiae: Volume 38*. Cambridge University Press: Cambridge.

Ásgeirsdóttir, H.G., Valdimarsdóttir, U.A., Þorsteinsdóttir, P.K., Lund, S.H., Tomasson, G., Nyberg, U., Ásgeirsdóttir, T.L., Hauksdóttir, A., 2018. The association between different traumatic life events and suicidality. Eur. J. Psychotraumatol. 9(1), 1510279. http://doi:10.1080/20008198.2018.1510279.

Augustine of Hippo (2008). *The City of God*. Hendrickson Publishers: New York.

Australian Bureau of Statistics. The health and welfare of Australia's aboriginal and Torre Strait Islander People. Australian Bureau of Statistics, Camberra. Retrived online,2005; http://www.abs.gov.au/a 2005.

Ayesa-Arriola R, Canal Rivero M, Delgado-Alvarado M, Setién-Suero E, González-Gómez J, Labad J, et al. Low-density lipoprotein cholesterol and suicidal behaviour in a large sample of first-episode psychosis patients. World J Biol Psychiatry (2018) 11:1-4. https://doi:10.1080/15622975.2017.1414305.

Baek JH, Kang ES, Fava M, Mischoulon D, Nierenberg AA, Yu BH, et al. Serum lipids, recent suicide attempt and recent suicide status in patients with major depressive disorder. Progr NeuroPsychopharmacol Biol Psychiatry. (2014) 51:113-8. https://doi:10.1016/j.pnpbp.2014.01.018.

Baldessarini, R.J., Vázquez, G.H., Tondo, L., 2016. Affective temperaments and suicidal ideation and behavior in mood and anxiety disorder patients. J. Affect. Disord. 198, 78-82.

Balint, M. (1959). Thrills and Regressions. London: Routledge.

Balint, M. (1968). The Basic Fault. London: Tavistock.

Bando, D.H., Teng, C.T., Volpe, F.M., de Masi, E., Pereira, L.A., Braga, A.L., 2017. Suicide and meteorological factors in Sao Paulo, Brazil, 1996-2011: a time series analysis. Rev. Bras. Psiquiatr. 39, 220-227. http://doi:10.1590/1516-4446-2016-2057.

Baraff, L. J., Janowicz, N., Asarnow, J. R. Survey of California emergency departments about practices for management of suicidal patients and resources available for their care. Ann. Emerg. Med., 2006; 48: 452-8.

Barak, Y., Baruch, Y., Achiron, A., Aizenberg, D. Suicide attempts of schizophrenia patients: A case-controlled study in tertiary care. J. Psych. Res., 2008; 42: 822-26.

Barbagli M. (2009). *Congedarsi dal mondo*. [*Leaving the world*]. Il Mulino: Milan.

Barr W., Leitner M., Thomas J. Psychosocial assessment of patients who attend an accident and emergency department with self-harm. J. Psychiatr. Ment. Health Nurs., 2005; 12: 130-8.

Bartoli F, Crocamo C, Dakanalis A, Riboldi I, Miotto A, Brosio E, et al. Association between total serum cholesterol and suicide attempts in subjects with major depressive disorder: exploring the role of clinical and biochemical confounding factors. Clin Biochem. (2017) 50(6):274-8. https://doi:10.1016/j.clinbiochem.2016.11.035.

Batty, G.D., Gale, C.R., Tanji, F., Gunnell, D., Klvimaki, M., Tsuji, I., Jokela, M., 2018. Personality traits and risk of suicide mortality: findings from a multi-cohort study in the general population. World. Psychiatry. 17(3), 371-372. http://doi:10.1002/wps.20575.

Beautrais AL. Suicides and serious suicide attempts: two populations or one? Psychol Med. (2001) 31(5):837-45.

Beautrais, A. L. Suicides and serious suicide attempts in youth: a multiple-group comparison study. Am. J. Psychiatry, 2003; 160: 1093–99.

Bech, P., Awata, S. Measurement of suicidal behavior with psychometric scales. In: Wassermann D., Wassermann C. ed., Oxford Textbook of Suicidology and Suicide Prevention. Oxford: Oxford University Press 2009.

Becker, S.P., Holdaway, A.S., Luebbe, A.M. 2018. Suicidal behaviors in college students: frequency, sex differences, and mental health correlates including sluggish cognitive tempo. J. Adolesc. Health. 63(2), 181-188.

Bekry, A. A. Trends in suicide, parasuicide and accidental poisoning in Addis Ababa, Ethiopia. Ethiop. J. Health Dev., 1999; 13(3): 247-62.

Bennewith, O., Stocks, N., Gunnell, D., Peters, T. J., Evans, M. O., Sharp, D. J. General practice based intervention to prevent repeat episodes of deliberate self-harm: cluster randomized controlled trial. B.M.J., 2002; 324: 1254-57.

Berman L. (2012). *News bulletin, IASP*. October- November 2012.

Bertolote, J. M. Suicide in the world: an epidemiological overview 1959-2000. In: Wassermann D. ed., Suicide an unnecessary death. London: Martin Dunitz 2001.

Bertolote, J. M., Fleischmann, A., De Leo, D., Bolhari, J., Botega, N., De Silva, D., et al. Suicide attempts, plans, and ideation in culturally diverse sites: the WHO SUPRE-MISS community survey. Psychol. Med., 2010; 35(10): 1457-65.

Bertolote, J. M., Wasserman D. Developments of definitions of suicidal behaviours. In: Oxford Textbook of Suicidology and Suicide Prevention. Oxford: Oxford University Press 2009.

Beşirli, A., 2018. The relationship between impulsivity and panic disorder-agoraphobia: The role of affective temperament. Psychiatry. Res., 264, 169-174.

Bille-Brahe, U., Kerkhof, A. J. F. M., Leo, D. D., Schmidtke, A., Crepet, P., Lönnqvist, J., et al. A repetition-prediction study of European parasuicide populations: a summary of the first report from Part I1 of the WHO/EURO Multicentre Study on Parasuicide in co-operation with the EC Concerted Action on Attempted Suicide. Acta Psychiatr. Scand., 1997; 95: 81-86.

Bille-Brahe, U., Schmidtke, A., Kerhof, A. Background and introduction to the study. In: Kerkhof A., Schmidtke A., Bille- Brahe U. eds, Attempted suicide in Europe. Findings from the Multicentre Study on Parasuicide by the WHO Regional Office for Europe, pp. 3- 15. Leiden: DSWO Press 1964.

Bion, W. R. (1959). Attacks on linking. Int. J. Psychoanal., 40:308-315.

Bion, W.R. (1958). On Arrogance. Int. J. Psycho-Anal., 39:144-146.

Black, D. W., Blum, N., Pfohl, B., Hale, N. Suicidal behavior in borderline personality disorder: prevalence, risk factors, prediction, and prevention. J. Pers. Disord., 2004; 18(3): 226-239.

Blacker, C.J., Lewis, C.P., Swintak, C.C., Bostwick, J.M., Rackley, S.J. 2018. Medical Student Suicide Rates: A Systematic Review of the Historical and International Literature. Acad. Med. [Epub ahead of print]

Bolton, J. M., Belik, S. L., Enns, M. W., Cox, B. J., Sareen, J. Exploring the correlates of suicide attempts among individuals with major depressive disorder: findings from the national epidemiologic survey on alcohol and related conditions. J. Clin. Psychiatry, 2008; 69: 1139–49.

Bolton, J. M., Pagura, J., Enns, M. W., Grant, B., Sareen, J. A population based longitudinal study of risk factors for suicide attempts in major depressive disorder. J. Psychiatr. Res., 2010; 44(13): 817–26.

Bortolato, M., Pivac, N., Seler, D. M., Nikolac Perkovic, M., Pessia, M., Di Giovanni, G. The role of the serotonergic system at the interface of aggression and suicide. Neuroscience, 2013; 236: 160-85.

Botega, N. J., Barros, M. B., Oliveira, H. B., Dalgalarrondo, P., Marín-León, L. Suicidal behavior in the community: prevalence and factors associated with suicidal ideation. Rev. Bras. Psiquiatr., 2005; 27(1): 45-53.

Bradvik, L., Berglund, M. Repetition and severity of suicide attempts across the life cyrcle: a comparison by age group between suicide victims and controls with severe depression. B.M.C. Psychiatry, 2009; 9:62-72.

Brent, D. A., Melhem, N. Familial transmission of suicidal behavior. Psych. Clin. North Am., 2008; 31(2): 157-77.

Brent, D. A., Moritz, G. Developmental pathways to adolescent suicide. In: D. Chichetti, S. Toth (Eds.), Adolescents: opportunities and challenges. New York: University of Rochester Press 1996.

Breuer C. (2015). Unemployment and suicide mortality: evidence from regional panel data in Europe. *Health economics* 24(8), 936-950.

Brewerton, T.D., Putnam, K.T., Lewine, R.R.J., Risch, S.C., 2018. Seasonality of cerebrospinal fluid monoamine metabolite concentrations and their associations with meteorological variables in humans. J. Psychiatr. Res. 99, 76-82. http://doi:10.1016/j.jpsychires.2018.01.004.

Brezo, J., Paris, J., Hébert, M., Vitaro, F., Tremblay, R., Turecki, G. Broad and narrow personality traits as markers of one-time and repeated suicide attempts: a population-based study. B.M.C. Psychiatry, 2008; 8: 5-11.

Brickman, A. L., Mintz, D. C. US rates of self-inflicted injuries and suicide, 1992–1999. Psych. Serv., 2003; 54(2): 168-73.

Brodsky, B. S., Mann, J. J., Stanley, B., Tin, A., Oquendo, M., Birmaher, B., et al. Familial transmission of suicidal behavior: factors mediating the relationship between childhood abuse and offspring suicide attempts. J. Clin. Psychiatry, 2008; 69(4), 584.

Brown RM. (2001). *The art of suicide*. Reaction Books: London.

Brown, G. K., Jeglic, E., Beck, A. T. Cognitive Therapy, Cognition, and Suicidal Behavior. In: Ellis ed.: Cognition and suicide: theory, research and therapy. Washington: American Psychological Association 2006.

Burrows J. (1828). *Commentaries on the causes, forms, symptoms and treatment, moral and medical, of insanity*. Thomas and George Underwood ed.: London

Canetto, S. S. Meanings of gender and suicidal behaviour during adolescence. Suicide Life Threat. Behav., 1997; 27 (4): 339-51.

Canner, J.K., Giuliano, K., Selvarajah, S., Hammond, E.R., Schneider, E.B., 2018. Emergency department visits for attempted suicide and self-harm in the USA: 2006–2013. Epidemiol. Psychiatr. Sci. 27(1), 94-102. http://doi:10.1017/S2045796016000871.

Carleton, T.A., 2017. Crop-damaging temperatures increase suicide rates in India. Proc. Natl. Acad. Sci. USA. 114(33), 8746-8751. http://doi/10.1073/pnas.1701354114.

Carter, T. D., Mundo, E., Parikh, S. V., Kennedy, J. L. Early age at onset as a risk factor for poor outcome of bipolar disorder. J. Psychiatr. Res., 2003; 37:297–303.

Carver, C.S., Scheier, M.F., Weintraub, J.K., 1989. Assessing coping strategies: a theoretically based approach. J. Pers. Soc. Psychol. 56, 267-283.Campos, R.C., Holden, R.R., Costa, F., Oliveira, A.R., Abreu, M., Fresca, N., 2017. The moderating effect of gender on the relationship between coping and suicide risk in a Portuguese community sample of adults. J. Ment. Health. 26(1), 66-73.

Casas, L., Cox, B., Bauwelinck, M., Nemery, B., Deboosere, P., Nawrot T.S., 2017. Does air pollution trigger suicide? A case-crossover analysis of suicide deaths over the life span. Eur. J. Epidemiol. 32(11), 973-981. http://doi:10.1007/s10654-017-0273-8.

Cavanagh, J.T.O., Carson, A. J., Sharpe, M., Lawrie, S. M. Psychological autopsy studies of suicide: a systematic review. Psychol. Med., 2003;33: 395–405.

CDC (Center for disease control and prevention). Youth Risk Behaviour Surveillance – USA 2011.MMWR, 2012; 61 (4), 8th June 2012.

CDC (Centers for Disease Control and Prevention). Suicide and Attempted Suicide - China, 1990-2002 Morbidity and Mortality Weekly Report 53; 481-484 retrieved online on 7 April 2013 at http://www.cdc.gov/mmwR/preview/mmwrhtml/mm5322a6.htm 2004.

Champagne, D. L., Bagot, R. C., van Hasselt, F., Ramakers, G., Meaney, M. J., De Kloet, E. R., et al. Maternal care and hippocampal plasticity: evidence for experience-dependent structural plasticity, altered synaptic functioning, and differential responsiveness to glucocorticoids and stress. J. Neuroscience, 2008; 28(23): 6037-45.

Chandrasekaran, R., Gnananselane, J. Predictors of repeat suicidal attempt after first-ever attempt: a two-year follow-up study. Hong Kong J. Psychiatry, 2008; 18:131-135.

Chang JC, Yen AM, Lee CS, Chen SL, Chiu SY, Fann JC, et al. Metabolic syndrome and the risk of suicide: a community-based integrated screening samples cohort study. Psychosom Med. (2013) 75(9):807-14. https://doi:10.1097/PSY.0000000000000014.

Chen VC, Cheng AT, Tan HK, Chen CY, Chen TH, Stewart R, et al. A community-based study of case fatality proportion among those who carry out suicide acts. Soc Psychiatry Psychiatr Epidemiol. (2009) 44:1005-11. https://doi:10.1007/s00127-009-0021-9.

Chen, P. C., Lee, L. K., Wong, K. C., Kaur, J. Factors relating to adolescent suicidal behavior: a cross-sectional Malaysian school survey. J. Adolesc. Health, 2005; 37(4): 11-337.

Cheung, Y. B., Law, C. K., Chan, B., Liu, K. Y., Yip, P. S. Suicidal ideation and suicidal attempts in a population-based study of Chinese people: risk attributable to hopelessness, depression, and social factors. J. Affect. Disord., 2006; 90(2-3): 193-99.

Chevalier T. (1824). Remarks on suicide. *The Pampheleteer* 23, 365-73

Chien, W. C., Lai, C. H., Chung, C. H. A nation- wide evidence- based analysis of repeated suicide attempts. Crisis, 2013; 34(1): 22-31.

Christiansen, E., Frank Jensen, B. Risk of repetition of suicide attempt, suicide or all deaths after an episode of attempted suicide: a register-based survival analysis. Australasian Psych., 2007; 41(3): 257-65.

Christodoulou, C., Douzenis, A., Papadopoulos, F.C., Papadopoulou, A., Bouras, G., Gournellis, R., Lykouras, L., 2012. Suicide and seasonality. Acta. Psychiatr. Scand. 125, 127-146. http://doi:10.1111/j.1600-0447.2011.01750.x.

Churchill L R. (1994). Physician-assisted suicide. *Journal of the Royal Society of Medicine* 87, 44-46.

Claassen, C. A., Trivedi, M. H., Rush, A. J., Husain, M. M., Zisook, S., Young, E. Clinical differences among depressed patients with and without a history of suicide attempts: findings from the STAR*D trial. J. Affect. Disord., 2007; 97:77–84.

Claassen, C. A., Trivedi, M. H., Shimizu, I., Stewart, S., Larkin, G. L., Litovitz, T. Epidemiology of nonfatal deliberate self-harm in the United States as described in three medical databases. Suicide Life Threat. Behav., 2006; 36: 192-212.

Coimbra, D.G., Pereira E Silva, A.C., de Sousa-Rodrigues, C.F., Barbosa, F.T., de Siqueira Figueredo, D., Araùjo Santos, J.L., Barbosa, M.R., de Medeiros Alves, M., Nardi, A.E., de Andrade, T.G., 2016. Do suicide attempts occur more frequently in the spring too? A systematic review and rhythmic analysis. J. Affect. Disord. 196, 125-137. http://doi:10.1016/j.jad.2016.02.036.

Corcoran, P., Keeley H. S., O'Sullivan, M., Perry, I. J. The incidence and repetition of attempted suicides in Ireland. Eur. J. Public Health, 2004; 14 (1): 19-23.

Costa Lda, S., Alencar, A.P., Nascimento Neto, P.J., dos Santos Mdo, S., da Silva, C.G., Pinheiro Sde, F., Silveira, R.T., Bianco, B.A., Pinheiro, R.F. Jr., de Lima, M.A., Reis, A.O., Rolim Neto, M.L., 2015. Risk factors for suicide in bipolar disorder: a systematic review. J. Affect. Disord. 170, 237-254. http://doi:10.1016/j.jad.2014.09.003

Costello E J, Compton S N, Keeler G, Angold A. (2003). Relationships between poverty and psychopathology: A natural experiment. *JAMA* 290(15), 2023-2029.

Courtet P, Jaussent I, Genty C, Dupuy AM, Guillaume S, Ducasse D, et al. Increased CRP levels may be a trait marker of suicidal attempt. Eur Neuropsychopharmacol. (2015) 25(10):1824-31. https://doi:10.1016/j.euroneuro.2015.05.003.

Courtet, P. , Thuile, J. Les suicidants multirécidivistes: une population particulère? Suicides et tentatives de suicide. Paris: Médecine-Sciences Flammarion, pp. 26–31, 2010.

Courtet, P., Jollant, F., Buresi, C., Castelnau, D., Mouthon, D., Malafosse, A. The monoamine oxidase A gene may influence the means used in suicide attempts. . The monoamine oxidase A gene may influence the means used in suicide attempts. Psychiatr. Genet., 2005; 15(3): 189-93.

Crone D M. (1996). Historical Attitudes Toward Suicide. *Duquesne Law Review* 35, 7-42.

Crumlish, N., Whitty, P., Kamali, M., Clarke, M., Browne, S., McTigue, O., et al. Early insight predicts depression and attempted suicide after 4 years in first-episode schizophrenia and schizophreniform disorder. Acta Psych. Scand., 2005; 112:449–55.

Da Silva Cais, C. F., Stefanello, S., Fabrício Mauro, M. L., Vaz Scavacini de Freitas, G., Botega, N. J. Factors associated with repeated suicide attempts. Preliminary results of the WHO Multisite Intervention Study non Suicidal Behavior (SUPRE-MISS) from Campinas, Brazil. Crisis, 2009; 30: 73–8.

Daray FM, Mann JJ, Sublette ME. How lipids may affect risk for suicidal behavior. J Psychiatr Res. (2018) 104:16-23. https://doi:10.1016/j.jpsychires.2018.06.007.

De Leo, D., Burgis, S., Bertolote, J. M., Kerkhof, A. J., Bille-Brahe, U. Definitions of suicidal behavior. Crisis, 2006; 27(1): 4-15.

De Leo, D., Milner, A., Sveticic, J. Mental Disorders and Communication of Intent to Die in Indigenous Suicide Cases, Queensland, Australia. Suicide Life Threat. Behav., 2012; 42(2): 57-64.

De Vogli R, Marmot M, Stuckler D. (2013). Excess suicides and attempted suicides in Italy attributable to the great recession. *Journal of epidemiology and community health* 67(4), 378-379.

Deisenhammer, E. A., Strauss, R., Kemmler, G., Hinterhuber, H., Weiss, E. M. The duration of the suicidal process: how much time is left for intervention between consideration and accomplishment of a suicide attempt? J. Clin. Psychiatry, 2009; 70(1): 19-24.

Dejong, T.M., Overholser, J. C., Stockmeier, C.A. Apples to oranges?: A direct comparison between suicide attempters and suicide completers. J. Affect. Disord., 2010; 124: 90–97.

Deonarain, M., Pillay, B. J. A study of parasuicide behaviour at the Chris Hani Baragwanath Hospital. Suicid. Behav., 2000; 4: 112-27.

DeRijk, R. H., van Leeuwen, N., Klok M. D., Zitman, F. G. Corticosteroid receptor-gene variants: Modulators of the stress-response and implications for mental health. Eur. J. Pharmacol., 2008; 585 (2–3): 492-501.

DeShong, H.L., Tucker, R.P., O'Keefe, V.M., Mullins-Sweatt, S.N., Wingate, L.R., 2015. Five factor model traits as a predictor of suicide ideation and interpersonal suicide risk in a college sample. Psychiatry. Res. 226(1), 217-223. http://doi:10.1016/j.psychres.2015.01.002.

Dickerson F, Adamos M, Katsafanas E, Khushalani S, Origoni A, Savage C, et al. The association between immune markers and recent suicide attempts in patients with serious mental illness: a pilot study. Psychiatry Res. (2017) 255:8-12. https://doi:10.1016/j.psychres.2017.05.005.

Dixon, P.G., Kalkstein, A.J., 2018. Where are weather-suicide associations valid? An examination of nine US counties with varying seasonality. Int. J. Biometeorol. 62(5), 685-697. http://doi:10.1007/s00484-016-1265-1.

Doganay, Z., Sunter, A.T., Guz, H., Ozkan, A., Altintop, L., Kati, C., Colak, E., Aygun, D., Guven, H., 2003. Climatic and diurnal variation in suicide attempts in the ED. Am.

J. Emerg. Med. 21, 271-275.

Dolev N. (1999). Gaspar Ofhuys' Chronicle and Hugo van der Goes. *Assaph: Publication of the Tel-Aviv University, Faculty of Fine Arts. Studies in art history* 4, 125.

Domino, G., 1981. Attitude toward suicide among Mexican American and Anglo youth. Hisp. J. Behav. Sci. 3, 385-395.

Domino, G., 2005. Cross-cultural attitudes towards suicide: the SOQ and a personal odyssey. Arch. Suicide. Res. 9(2), 107-122.

Domino, G., Domino, M., Su, A., 2001-2002. Psychosocial aspects of suicide in young Chinese rural women. OMEGA. 44, 223-241.

Domino, G., Gibson, L., Poling, S., Westlake, L., 1980. Students' attitudes towards suicide. Soc. Psychiatry. 15: 127-130.

Domino, G., Perrone, L., 1993. Attitudes toward Suicide: Italian and United States Physicians. OMEGA. 27, 195-206.

Domino, G., Sulin, S., Shen, D., 2000. Cross-cultural investigation of a new set of scales for the Suicide Opinion Questionnaire. OMEGA. 41(4), 307-321.

Duberstein, P. R., Conwell, Y., Seidlitz, L., Denning, D. G., Cox, C., Caine, E. D. Personality traits and suicidal behavior and ideation in depressed inpatients 50 years of age and older. J. Gerontol. B. Psychol. Sci. Soc. Sci., 2000; 55:18–26.

Durkheim E. (1897). *Suicide, a study in sociology*. Free Press: New York.

Dwivedi, Y., Pandey, G. N. Elucidating biological risk factors in suicide: Role of protein kinase A. Prog. Neuropsychopharmacol. Biol. Psych., 2011; 35(4): 831-41.

Dwivedi, Y., Rizavi, H. S., Conley, R. R., Roberts, R. C., Tamminga, C. A., Pandey, G. N. Altered gene expression of brain-derived neurotrophic factor and receptor tyrosine

kinase B in postmortem brain of suicide subjects. Arch. Gen. Psychiatry, 2004; 60(8): 804-15.

Dyrbye, L.N., Thomas, M.R., Massie, F.S., Power, D.V., Eacker, A., Harper, W., Durning, S., Moutier, C., Szydlo, D.W., Novotny, P.J., Sloan, J.A., Shanafelt, T.D., 2008. Burnout and suicidal ideation among U.S. medical students. Ann. Intern. Med. 149(5), 334-341.

Economou M, Madianos M, Peppou L E, Theleritis C, Stefanis C N. (2012). Suicidality and the economic crisis in Greece. *The Lancet*, 380(983), 337.

Elias, L.R., Köhler, C.A., Stubbs, B., Maciel, B.R., Cavalcante, L.M., Vale, A.M., Gonda, X., Quevedo, J., Hyphantis, T.N., Soares, J.C., Vieta, E., Carvalho, A.F., 2017. Measuring affective temperaments: a systematic review of validation studies of the Temperament Evaluation in Memphis Pisa and San Diego (TEMPS) instruments. J. Affect. Disord. 212, 25-37.

Emmelkamp, P. M. The additional value of clinimetrics needs to be established rather than assumed. Psychother. Psychosom., 2004; 73(3): 142-144.

Esquirol J. (1821). Suicide, In: *Dictionnaire des Sciences Médicales: par une societé des medécins et des chirurgiciens*, vol. LIII. Panckouke: Paris.

Evans, E., Hawton, K., Rodham, K. Suicidal phenomena and abuse in adolescents: a review of epidemiological studies. Child Abuse Negl., 2005; 29(1): 45-58.

Farberow N L. (1975). *Suicide in different cultures*. University Park Press: New York.

Fazakas-DeHoog, L.L., Rnic, K., Dozois, D.J., 2017. A cognitive distortions and deficits model of suicide ideation. Eur. J. Psychol. 13(2), 178-193.

Feldman, M. (2008). Grievance: The underlying oedipal configuration. Int. J. Psycho-Anal., 89(4): 743-758.

Fergusson, D. M., Boden, J. M., Horwood, L. J. Exposure to childhood sexual and physical abuse and adjustment in early adulthood. Child Abuse Negl., 2008; 32(6): 607-19.

Fergusson, D. M., Woodward, L. J., Horwood, L. J. Risk factors and life processes associated with the onset of suicidal behaviour during adolescence and early adulthood. Psychol. Med., 2000; 30: 23–39.

Fiedorowicz JG, Coryell WH. Cholesterol and suicide attempts: a prospective study of depressed inpatients. Psychiatry Res. (2007) 152(1):11-20.

Fleischmann, A., Bertolote, J. M., De Leo, D., Botega, N., Phillips, M., Sisask, M., et al. Characteristics of attempted suicides seen in emergency care settings of general hospitals in eight low and middle income countries. Psychol. Med., 2005; 35(10): 1467-1474.

Fleming C. (1773). *A dissertation upon the unnatural crime of self-murder*. Dilly:London.

Flink, N., Lehto, S.M., Koivumaa-Honkanen, H., Viinamäki, H., Ruusunen, A., Valkonen-Korhonen, M., Honkalampi, K., 2017. Early maladaptive schemas and suicidal ideation in depressed patients. Eur. J. Psychiatry. 31(3), 87-92.

Foley, D. L., Goldston, D. B., Costello, E. J., Angold, A. Proximal psychiatric risk factors for suicidality in youth: The Great Smoky Mountains study. Arch. Gen. Psychiatry, 2006; 63(9): 1017–24.

Fond, G., Faugere, M., Faget-Agius, C., Cermolacce, M., Richieri, R., Boyer, L., Lancon, C., 2018. Hypovitaminosis D is associated with negative symptoms, suicide risk, agoraphobia, impaired functional remission, and antidepressant consumption in schizophrenia. Eur. Arch. Psychiatry. Clin. Neurosci. [Epub ahead of print]. http://doi:10.1007/s00406-018-0932-0.

Foucault M. (1981). *The History of sexuality, vol. I, An Introduction*. Trans. Hurley R., Harmondsworth. Penguin: London.

Foucault M. (2002). *The Essential Works of Foucault 1954-1984*, vol. III: Power. London: Penguin.

Fountoulakis K N, Koupidis S A, Siamouli M, Grammatikopoulos I A, Theodorakis P N. (2013). Suicide, recession, and unemployment. *Lancet* 381(986), 721-722.

Fountoulakis, K. N., Chatzikosta, I., Pastiadis, K., Zanis, P., Kawohl, W., Kerkhof, A. J., & Rancans, E. (2016). Relationship of suicide rates with climate and economic variables in Europe during 2000–2012. Ann Gen Psych, 15(1), 19.

Fountoulakis, K.N., Savopoulos, C., Zannis, P., Apostolopoulou, M., Fountoukidis, I., Kakaletsis, N., Kanellos, I., Dimellis, D., Hyphantis, T., Tsikerdekis, A., Pompili, M., Hatzitolios, A.L., 2016. Climate change but not unemployment explains the changing suicidality in Thessaloniki Greece (2000-2012). J. Affect. Disord. 193, 331-338. http://doi:10.1016/j.jad.2016.01.008.

Franko, D. L., Keel, P. K., Dorer, D. J. Blais, M. A., Delinsky, S. S., Eddy, K. T., et al. What predicts suicide attempts in women with eating disorders? Psychol. Med., 2004; 34: 843-53.

Freeman, D. J., Wilson, K., Thigpen, J., McGee, R. K. Assessing intention to die in self-injury behavior. Psychol. Assess. Suicid. Risk, 1974; 494: 18-30.

Freemantle E, Mechawar N, Turecki G. Cholesterol and phospholipids in frontal cortex and synaptosomes of suicide completers: relationship with endosomal lipid trafficking genes. J Psychiatr Res. (2013) 47:272-9. https://doi:10.1016/j.jpsychires.2012.10.019.

Fullerton-Gleason, L. Suicide surveillance in Colorado. Analysis of hospital discharge data: Identifying characteristics associated with a second hospitalized suicide attempt.

Denver: The Injury Epidemiology Program, Colorado Department of Public Health and Environment 2005.

Fushimi, M., Sugawara, J., Saito, S. Comparison of completed and attempted suicide in Akita, Japan. Psychiatr. Clin. Neurosci., 2006; 60: 289–95.

Gadalla T M. (2009). Determinants, correlates and mediators of psychological distress: A longitudinal study. *Social science and medicine* 68,12: 2199-2205.

Galvão, P.V.M., Silva, H.R.S.E., Silva C.M.F.P.D., 2018. Temporal distribution of suicide mortality: A systematic review. J. Affect. Disord. 228, 132-142. http://doi:10.1016/j.jad.2017.12.008.

Galynker, I., Yaseen, Z.S., Briggs, J., Hayashi, F., 2015. Attitudes of acceptability and lack of condemnation toward suicide may be predictive of post-discharge suicide attempts. BMC Psychiatry. 15, 87.

Gao, J., Cheng, Q., Duan, J., Xu, Z., Bai, L., Zhang, Y., Zhang, H., Wang, S., Zhang, Z., Su, H. 2019. Ambient temperature, sunlight duration, and suicide: A systematic review and meta-analysis. Sci. Total. Environ. 646, 1021-1029. http://doi:10.1016/j.scitotenv.2018.07.098.

George M D. (1951). *London life in the eighteenth century*. Routledge: London.

Germain, A., Kupfer, D.J., 2008. Circadian rhythm disturbances in depression. Hum. Psychopharmacol. 23, 571-585. http://doi:10.1002/hup.964.

Gibbs J P, Martin W T. (1958), A Theory of Status Integration and its Relationship to Suicide. *American Sociological Review* 23, 140-147

Giegling, I., Olgiati, P., Hartmann, A. M., Calati, R., Möller, H. J., Rujescu, D. Personality and attempted suicide. Analysis of anger, aggression and impulsivity. J. Psychiatr. Res., 2009; 43: 1262–71.

Gillberg, C. A guide to Asperger syndrome. London: Cambrige University Press 2002.

Gmitrowicz, A., Szymczak, W., Kotlicka-Antczak, M. Suicidal ideation and suicide attempt in Polish adolescents: is it a suicidal process?. Int. J. Adolesc. Med. Health, 2003; 15(2): 113-24.

Goldney, R. D., Smith, S., Winefield, A. H., Tiggeman, M., Winefield, H. R. (1991). Suicidal ideation: its enduring nature and associated morbidity. Acta Psych. Scand., 83(2): 115-120.

Goldston, D. B., Daniel, S. S., Reboussin, B. A., Reboussin, D. M., Kelley, A. E., Frazier, P. H. Psychiatric diagnoses of previous suicide attempters, first-time attempters, and repeat attempters on an adolescent inpatient psychiatry unit. J. Am. Acad. Child Adolesc. Psych., 1998; 37: 924–32.

Goldston, D. B., Reboussin, B. A., Daniel, S. S. Predictors of suicide attempts: State and trait components. J. Abnorm. Psychol., 2006; 115(4): 842–849.

Gonda, X., Fountoulakis, K.N., Harro, J., Pompili, M., Akiskal, H.S., Bagdy, G., Rihmer, Z., 2011. The possible contributory role of the S allele of 5-HTTLPR in the emergence of suicidality. J. Psychopharmacol. 25, 857-866.

Gotlib, I. H., Joormann, J., Minor, K. L., Hallmayer, J. HPA-Axis reactivity: A mechanism underlying the associations among 5-HTTLPR, stress, and depression. Biol. Psychiatry., 2008; 63(9): 847-851.

Gottesman, I. I., Gould, T. D. The endophenotype concept in psychiatry: etymology and strategic intentions. Am. J. Psychiatry., 2005; 160(4): 636-45.

Gould, M.S., Lake, A.M., Kleinman, M., Galfalvy, H., Chowdhury, S., Madnick, A., 2018. Exposure to suicide in high schools: impact on serious suicidal ideation/behavior, depression, maladaptive coping strategies, and attitudes toward help-seeking. Int. J. Environ. Res. Public. Health. 15(3), 455.

Green, A. (1993). The work of the negative. New York: Free Association Books.

Green, A. (1996). On Private Madness. London: Karnac.

Green, A. (1999). Passivité-passivation: Jouissance et détresse. [Passivity-passivation: enjoyment and distress]. Rev. Fr. Psychoanal., 63(3): 1587-1600.

Grjibovski, A.M., Kozhakhmetova, G., Kosbayeva, A., Menne, B., 2013. Associations between air temperature and daily suicide counts in Astana, Kazakhstan. Medicina (Kaunas). 49(8), 379-385.

Groholt, B., Ekeberg, O. Prognosis after adolescent suicide attempt: mental health, psychiatric treatment, and suicide attempts in a nine year follow-up study. Suicide Life Threat. Behav., 2009; 39: 125–136.

Gvion, Y., Levi-Belz, Y., 2018. Serious Suicide Attempts: Systematic Review of Psychological Risk Factors. Front. Psychiatry. 9, 56. http://doi:10.3389/fpsyt.2018.00056

Hacking I. (1990). *The taming of chance*. Cambridge University Press: Cambridge.

Hakko, H., Rasanen, P., Tiihonen, J., 1998. Seasonal variation in suicide occurrence in Finland. Acta. Psychiatr. Scand. 98(2), 92-97.

Halbwachs M. (1930). *Les causes du suicide*. Alcan ed.: Paris.

Hamermesh D S, Soss N M. (1974). An economic theory of suicide. *Journal of political economy*, 83-98

Hantouche, E.G., Akiskal, H.S., 2005. Toward a validation of tripartite concept of a putative anxious temperament: psychometric data from a French national general medical practice study. J. Affect. Disord. 85, 37-43.

Haukka, J., Suominen, K., Partonen, T., Lönnqvist, J. Determinants and outcomes of serious attempted suicides: a nationwide study in Finland from 1996-2003. Am. J. Epidemiol., 2008; 67(10): 1155-63.

Hawton K, Van Heeringen K. (2009) Suicide. *Lancet* 373: 1372-1381.

Hawton, K. Completed suicides after attempted suicides: methods used in attempts may indicate the degree of risk. B. M. J., 2010; 341: 158-9.

Hawton, K., Arensman, E., Wasserman, D., Hulten, A., Bille-Brahe, U., Bjerke T., et al. Relation between attempted suicides and suicide rates among young people in Europe. J. Epidemiol. Comm. Health, 1998; 52: 191- 94.

Hawton, K., Sutton, L., Haw, C., Sinclair, J., Deeks, J. J. Schizophrenia and suicide: systematic review of risk factors. Br. J. Psichiatry, 2005; 187(1): 9-20.

Hawton, K., Van Heeringen, K. Suicide. Lancet, 2009; 373: 1372-81.

Hawton, K., van Heeringen, K., 2009. Suicide. Lancet. 373, 1372-1381. SEP http://doi:10.1016/S0140-6736(09)60372-X.

Hawton, K., Zahl D., Weatherall, R. Suicide following deliberate self-harm: long-term follow-up of patients who presented to a general hospital. Br. J. Psichiatry, 2003; 182: 537-42.

Hazlerigg, D.G., Andersson, H., Johnston, J.D., Lincoln, G., 2004. Molecular characterization of the long-day response in the Soay sheep, a seasonal mammal. Curr. Biol. 14(4), 334-339.

Head, L, Campbell-Hewson, G. L., O'Keane, V. No harm done? Psychological assessment in the A&E department of patients who deliberately harm themselves. J. R. Coll. Physicians Lond., 1999; 33:51-5.

Health Canada. Unintentional and intentional injury profile for aboriginal people in Canada. Health Canada, Ottawa. Online: http://www.hc-sc.gc.ca/index-eng.php 2001.

Healy R. (2006). Suicide in early modern and modern Europe. *Historical Journal* 49, 903-19

Heffer, T., Willoughby, T., 2017. A count of coping strategies: a longitudinal study investigating an alternative method to understanding coping and adjustment. PloS One. 12(10), e0186057.

Heila, H., Lonnqvist, J. The clinical epidemiology of suicide in schizophrenia. In: Murray R., Jones P., Susser E., Van Os, J., Cannon, M., eds., The Epidemiology of Schizophrenia, pp. 288-316. Cambridge University Press: Cambridge 2002.

Heim, C., Nemeroff, C. B. The role of childhood trauma in the neurobiology of mood and anxiety disorders: preclinical and clinical studies. Biol. Psychiatry, 2001; 49(12): 1023-39.

Helama, S., Holopainen, J., Partonen, T., 2013. Temperature-associated suicide mortality: contrasting roles of climatic warming and the suicide prevention program in Finland. Environ. Health. Prev. Med. 18(5), 349-355. http://doi.org/10.1007/s12199-013-0329-7.

Helps, Y., Harrison J. Hospitalized injury of Australia's aboriginal and Torres Strait Islander People. A.I.H.W. catalogue. 2006; 94.

Henry A F, Short J F. (1954). *Suicide and homicide: Some economic, sociological and psychological aspects of aggression* (Vol. 91442). Free Press: New York.

Hesketh, T., Ding, Q. J., Jenkins, R. Suicide ideation in Chinese adolescents. Soc. Psychiatry Psychiatr. Epidemiol., 2002; 37: 230–5.

Hill T D. (2004). *Ambitiosa Mors: suicide and the self in Roman thought and literature*. Routledge: London.

Hill, R. M., Castellanos, D., Pettit, J. W. Suicide-related behaviors and anxiety in children and adolescents: A review. Clin. Psychol. Rev., 2011; 31(7): 1133-44.

Hofstra, E., Elfeddali, I., Bakker, M., de Jong, J.J., van Nieuwenhuizen, C., van der

Feltz-Cornelis, C.M., 2018. Springtime Peaks and Christmas Troughs: A National Longitudinal Population-Based Study into Suicide Incidence Time Trends in the Netherlands. Front. Psychiatry. 9, 45. http://doi:10.3389/fpsyt.2018.00045.

Holmans, P., Weissman, M. M., Zubenko, G. S., Scheftner, W. A., Crowe, R. R., DePaulo Jr. Genetics of recurrent early-onset major depression (GenRED): final genome scan report. Am. J. Psychiatry, 2007; 164(2): 248-58.

Holopainen, J., Helama, S., Partonen, T., 2014. Does diurnal temperature range influence seasonal suicide mortality? Assessment of daily data of the Helsinki metropolitan area from 1973 to 2010. Int. J. Biometeorol. 58(6), 1039-1045. http://doi:10.1007/s00484-013-0689-0

Hoppit J. (1986). Financial Crises in Eighteenth-century England. *Economic History Review* 39(1), 39-58.

Horesh N, Levi-Belz Y, Apter A. Medically serious versus non-serious suicide attempts: Relationships of lethality and intent to clinical and interpersonal characteristics. J Affect Disord. (2012) 136:286-93. https://doi:10.1016/j.jad.2011.11.035.

Horesh, N., Levi, Y., Apter, A. Medically serious versus non-serious suicide attempts: Relationships of lethality and intent to clinical and interpersonal characteristics. J. Affect. Disord., 2012; 136(3): 286-93.

Horwitz, A.G., Czyz, E.K., Berona, J., King, C.A., 2018. Prospective Associations of Coping Styles With Depression and Suicide Risk Among Psychiatric Emergency Patients. Behav. Ther. 49, 225-236.

Houston R A. (2010) *Punishing the Dead?: Suicide, Lordship, and Community in Britain, 1500-1830*. Oxford University Press: Oxford.

Huang YC, Wu YW, Chen CK, Wang LJ. Methods of suicide predict the risks and method-switching of subsequent suicide attempts: a community cohort study in Taiwan. Neuropsychiatr Dis Treat. (2014) 10:711-8. https://doi:10.2147/NDT.S61965.

Huang, Y. Y., Cate, S. P., Battistuzzi, C., Oquendo, M. A., Brent, D., Mann, J. J. An association between a functional polymorphism in the monoamine oxidase a gene promoter, impulsive traits and early abuse experiences. Neuropsychopharmacol., 2004; 29: 1498-505.

Hung, C. F., Lung, F. W., Hung, T. H., Chong, M. Y., Wu, C. K., Wen, J. K., et al. Monoamine oxidase A gene polymorphism and suicide: an association study and meta-analysis. J. Affect. Disord., 2012; 136(3): 643-49.

Ichikawa, M., Inada, H., & Kumeji, M., 2014. Reconsidering the effects of blue-light installation for prevention of railway suicides. J Affect. Disord., 152, 183-185.

Imran, N., Tariq, K.F., Pervez, M.I., Jawaid, M., Haider, I.I., 2016. Medical students' stress, psychological morbidity, and coping strategies: a cross-sectional study from Pakistan. Acad. Psychiatry. 40(1), 92-96.

Innamorati M, Pompili M, Lester D. (2012) Economic crises and suicide. In: M. Pompili (Ed.) *Suicide: A Global Perspective*, pp. 30–39. Bentham Science: New York

Inoue, K., Tanii, H., Fukunaga, T., Abe, S., Nishimura, F., Kimura, Y., et al. The importance of the frequency of suicide attempts as a risk factor of suicide. J. Forensic Leg. Med., 2008; 15: 24–26.

Ishii, N., Terao, T., Araki, Y., Kohno, K., Mizokami, Y., Arasaki, M., Iwata, N., 2013. Risk factors for suicide in Japan: a model of predicting suicide in 2008 by risk factors of 2007. J. Affect. Disord. 147(1-3), 352-354. http://doi:10.1016/jad.2012.11.038.

Isometsä, E. T., Henriksson, M. M., Aro, H. M., Heikkinen, M. E., Kuoppasalmi, K. I., Lönnqvist, J. K. Suicide in major depression. Am. J. Psychiatry, 1994; 151: 530–6.

ISTAT Nota informativa "I suicidi in Italia: tendenze e confronti, come usare le statistiche" 08 agosto 2012. Accessibile online: www.istat.it 2012.

Jacobs, D., Douglas, G. The Harvard Medical School guide to suicide assessment and intervention. Jossey-Bass, 1999.

Jee, H.J., Cho, C.H., Lee, Y.J., Choi, N., An, H., Lee, H.J., 2017. Solar radiation increases suicide rate after adjusting for other climate factors in South Korea. Acta. Psychiatr. Scand. 135(3): 219-227. http://doi:10.1111/acps.12676

Jia, C. X., Wang, L. L., Xu, A. Q., Dai, A. Y., Qin, P. Physical illness and suicide risk in rural residents of contemporary China: a psychological autopsy case-control study. Crisis, 2014; 35(5): 330-7.

Johnson, J. G., Cohen, P., Gould, M. S., Kasen, S., Brown, J., Brook, J. S. Childhood adversities, interpersonal difficulties, and risk for suicide attempts during late adolescence and early adulthood. Arch. Gen. Psychiatry, 2002; 59: 741–749.

Johnson, R. L., Thomas, R. G., Thomas, K. E. State Injury Indicators Report, Third Edition–2004 Data Centers for Disease Control and Prevention, National Center for Injury Prevention and Control, Atlanta retrieved online on 07 April 2013 at: http://www.cdc.gov/injury/stateprograms/indicators_2004.html.

Joiner T. Why people die by suicide. Cambridge, MA: Harvard University Press (2007). 37

Joiner, Jr., T. E., Rudd, M. Intensity and duration of suicidal crises vary as a function of previous suicide attempts and negative life events. J. Consult. Clin. Psychol., 2000; 68: 909–16.

Jollant, F., Bellivier, F., Leboyer, M., Astruc, B., Torres, S., Verdier, R., et al. Impaired decision making in suicide attempters. Am. J. Psychiatry, 2005; 162(2): 304-10.

Joseph, A., Abraham, S., Muliyil, J. P., George, K., Prasad, J., Minz, S., et al. Evaluation of suicide rates in rural India using verbal autopsies, 1994–1999. B. M. J., 2003;326: 1121–2.

Kandel ER, Schwartz JH, Jessell TM, Siegelbaum SA, Hudspeth AJ, "Principles of Neural Science – Fifth Edition, Mc Graw Hill Medical, 2013.

Kapur, N., Cooper, J., King-Hele, S., Webb, R., Lawlor, M., Rodway, C., Appleby, L. The repetition of suicidal behavior: a multicenter cohort study. J. Clin. Psychiatry, 2006; 67: 1599–609.

Karam, E.G., Itani, L., Fayyad, J., Hantouche, E., Karam, A., Mneimneh, Z., Akiskal, H., Rihmer, Z., 2015. Temperament and suicide: A national study. J. Affect. Disord. 184, 123-128.

Karanikolos M, Mladovsky P, Cylus J, Thomson S, Basu S, Stuckler D, McKee M. (2013). Financial crisis, austerity, and health in Europe. *Lancet* 381(987), 1323-1331.

Kattimani, S., Bharadwaj, B., Sarkar, S., Mukherjee, A. Interrater Reliability of the Silverman., et al. Nomenclature for Suicide-Related Ideations, Behaviors, and Communications. Crisis, 2015; 36(1): 61-64.

Kattimani, S., Sarkar, S., Rajkumar, R.P., Menon, V., 2015. Stressful life events, hopelessness, and coping strategies among impulsive suicide attempters. J. Neurosci. Rural. Pract. 6(2), 171-176.

Kebede, D., Alem, A. Suicide attempts and ideation among adults in Addis Ababa, Ethiopia. Acta Psych. Scand., 1999; 397: 35-9.

Keilp, J. G., Gorlyn, M., Oquendo, M. A., Burke, A. K., Mann, J. J. Attention deficit in depressed suicide attempters. Psychiatr. Res., 159: 7-17.

Kelly, D. L., Shim, J. C., Feldman, S. M., Yu, Y., Conley, R. R. Lifetime psychiatric symptoms in patients with schizophrenia who died by suicide compared to others means of death. J. Psychiatr. Res., 2004; 38: 531-6.

Kentikelenis A , Karanikolos M, Reeves A, McKee M, Stuckler D. (2014). Greece's health crisis: from austerity to denialism. *Lancet* 383(991), 748-753.

Kerkhof, A. J., Bernasco, W., Bille-Brahe, U., Platt, S., Schmidtke, A. European parasuicide study interview schedule (EPSIS). Facts and figures: WHO/EURO.

Kessler, R. C., Borges, G., Walters, E. E. Prevalence of and risk factors for lifetime suicide attempts in the National Comorbidity Survey. Arch. Gen. Psychiatry, 1999; 56: 617-26.

Kienhorst, C. W. M., de Wilde, E. J., van den Bout, J., Broese van Groenou, M. I., Diekstra, R. F., Wolters, W. H. G. Self-Reported Suicidal Behavior in Dutch Secondary Education Students. Suicide Life Threat. Behav., 1990; 20(2): 101-13.

Kinyanda, E., Hjelmeland, H., Musisi, S. Deliberate self-harm as seen in Kampala, Uganda-a case control study. Soc. Psychiatry Psychiatr. Epidemiol,. 2004; 39: 318-25.

Kirkcaldy, B. D, Siefen, G. R., Urkin, J., Merrick, J. Risk factors for suicidal behavior in adolescents. Minerva Pediatr, 2006; 58:443–50.

Kjoller, M., Norlev, J., Davidsen, M. Recall bias and suicidal behavior in a six year follow-up study. In 10th European Symposium on Suicide and Suicidal Behaviour. Copenhagen, Denmark: National Institute of Public Health 2004.

Knafo, A., Guilé, J.M., Breton, J.J., Labelle, R., Belloncle, V., Bodeau, N., Boudailliez, B., De La Rivière, S.G., Kharij, B., Mille, C., Mirkovic, B., Pripis, C., Renaud, J., Vervel, C., Cohen, D., Gérardin, P., 2015. Coping strategies associated with suicidal

behaviour in adolescent inpatients with borderline personality disorder. Can. J. Psychiatry. 60(2 Suppl 1), S46-54.

Kodaka, M., Postuvan, V., Inagaki, M., Yamada, M., 2011. A systematic review of scales that measure attitudes towards suicide. Int. J. Soc. Psychiatry. 57(4), 338-361.

Kovacs D. (2002) *Volume V. Helen: Phoenician Women. Orestes*. Loeb Classical Library, Harvard University Press: Cambridge MA.

Kreitman, N. Parasuicide. Br. J. Psychiatry, 1969; 115 (523):747-56.

Krysinska, K., Lester, D. Post-traumatic stress disorder and suicide risk: a systematic review. Arch. Suicide Res., 2010; 14: 1–23.

Kselman T. (1988). Funeral conflicts in the nineteenth- century France. *Comparative Studies in sociology and history* 30 (2): 312-333.

Kumar, C.T., Mohan, R., Ranjith, G., Chandrasekaran, R. Gender differences in medically serious suicide attempts: A study from South India. Psychiatr. Res., 2006; 144: 79–86.

Kuo, C.J., Chen, W.Y., Tsai, S.Y., Chen, P.H., Ko, K.T., Chen, C.C., 2018. Excessive mortality and causes of death among patients with personality disorder with comorbid psychiatric disorders. Soc. Psychiatry. Psychiatr. Epidemiol. [Epub ahead of print]. http://doi:10.1007/s00127-018-1587-x.

Kurtulus Dereli, A., Demırci, G.N., Dodurga, Y., Özbal, S., Cankurt, U., Boz, B., Adiguzel, E., Acar, K., 2018. Evaluation of human pineal gland acetylserotonin O-methyltransferase immunoreactivity in suicide: A preliminary study. Med. Sci. Law. [Epub ahead of print]. http://doi:10.1177/0025802418797178.

Labonte, B., Turecki, G. The epigenetics of suicide: explaining the biological effects of early life environmental adversity. Arch. Suicide Res., 2010; 14(4): 291-310.

Laloë, V. Patterns of deliberate self-burning in various parts of the world: A review. Burns, 2004; 30 (3): 207-15.

Lalovic A, Levy E, Luheshi G, Canetti L, Grenier E, Sequeira A, et al. Cholesterol content in brains of suicide completers. Int J Neuropsychopharmacol. (2007) 10:159-66.

Lamis, D.A., Innamorati, M., Erbuto, D., Berardelli, I., Montebovi, F., Serafini, G., Amore, M., Krakow, B., Girardi, P., Pompili, M., 2018. Nightmares and suicide risk in psychiatric patients: The roles of hopelessness and male depressive symptoms. Psychiatry. Res. 264, 20-25.

Lavebratt, C., Sjoholm, L.K., Partonen, T., Schalling, M., Forsell, Y., 2010. PER2 variation is associated with depression vulnerability. Am. J. Med. Genet. B. Neuropsychiatr. Genet. 153B(2), 570-581. http://doi:10.1002/ajmg.b.31021.

Lee CY, Wu YW, Chen CK, Wang LJ. The rate of fatality and demographic characteristics associated with various suicide methods: a community-based study in Northern Taiwan. Crisis.(2014) 35:245-52. https://doi:10.1027/0227-5910/a000266.

Lee HJ, Kim YK. Serum lipid levels and suicide attempts. Acta Psychiatr Scand. (2003) 108(3):215-21.

Lee, H., Myung, W., Lee, C., Choi, J., Kim, H., Carroll, B.J., Kim, D.K., 2018. Clinical epidemiology of long-term suicide risk in a nationwide population-based cohort study in South Korea. J. Psychiatr. Res. 100, 47-55. http://doi:10.1016/j.jpsychires.2018.01.018

Leenaars, A. Suicide Notes. Human Sciences Press, New York 1988.

Lester D. (1968). Henry and Short on suicide: a critique. Journal of Psychology 70: 179-86

Lester D. (1992). A test of Durkheim's theory of suicide in primitive societies. Suicide and Life-threatening Behavior 22: 388-95

Levi, Y., Horesh, N., Fischel, T., Treves, I., Or, E., Apter, A. Mental pain and its communication in medically serious suicide attempts: an "impossible situation". J. Affect. Disord., 2008; 111: 244–50.

Levine, S.Z., Bakst, S., Rabinowitz, J. Suicide attempts at the time of first admission and during early course schizophrenia: a population based study. Psychiatry Res., 2010; 177: 55–9.

Levinson, D., Haklai, Z., Stein, N., Polakiewicz, J., Levav, I. Suicide ideation, planning and attempts: results from the Israel National Health Survey. Isr. J. Psychiatry, 2007; 44(2): 136-43.

Lewinsohn, P. M., Rohde, P., Seeley, J. R., Baldwin, C. L. Gender differences in suicide attempts from adolescence to young adulthood. J. Am. Acad. Child Adolesc. Psych., 2001; 40: 427–34.

Li, A., Huang, X., Hao, B., O'Dea, B., Christensen, H., Zhu, T., 2015. Attitudes towards suicide attempts broadcast on social media: an exploratory study of Chinese microblogs. Peer J. 3, e1209.

Li, X., Phillips, M.R., 2010. The acceptability of suicide among rural residents, urban residents, and college students from three locations in China: a cross-sectional survey. Crisis. 31(4), 183-193.

Likhvar, V., Honda, Y., Ono, M., 2011. Relation between temperature and suicide mortality in Japan in the presence of other confounding factors using time-series analysis with a semiparametric approach. Environ. Health. Prev. Med. 16(1), 36-43. http://doi:10.1007/s12199-010-0163-0.

Lin, H.C., Chen, C.S., Xirasagar, S., Lee, H.C., 2008. Seasonality and Climatic Associations with Violent and Nonviolent Suicide: A Population-Based Study. Neuropsychobiology. 57, 32-37. http://doi:10.1159/000129664

Lincoln, G.A., Andersson, H., Hazlerigg, D., 2003. Clock genes and the long-term regulation of prolactin secretion: evidence for a photoperiod/circannual timer in the pars tuberalis. J. Neuroendocrinol. 15(4), 390-397.

Lind V. (2004). Suicidal mind and body. Example from Northern Germany. In: Watt J.R., *From Sin to Insanity*. Cornell University Press: New York.

Linkowski, P., Martin, F., De Maertelaer, V., 1992. Effect of some climatic factors on violent and non-violent suicides in Belgium. J. Affect. Disord. 25, 161-166.

Liu X., Tein J.Y., Zhao Z., Sandler I. N. Suicidality and correlates among rural adolescents of China. J. Adolesc. Health, 2005; 37: 443–51.

Lloyd-Jones H. (1994). *Ajax, Electra, Oedipus Tyrannus*. Loeb Classical Library, Harvard University Press: Cambridge MA.

Loas G, Dalleau E, Lecointe H, Yon V. Relationships between anhedonia, alexithymia, impulsivity, suicidal ideation, recent suicide attempt, C-reactive protein and serum lipid levels among 122 inpatients with mood or anxious disorders. Psychiatry Res. (2016) 246:296-302. https://doi:10.1016/j.psychres.2016.09.056.

Lopez-Castroman, J., de las Mercedes Perez-Rodriguez, M., Jaussent, I., Alegria, A. A., Artes-Rodriguez, A., Freed, P., et al. Distinguishing the relevant features of frequent suicide attempters. J. Psychiatr. Res., 2011; 45: 619–25.

Lucero Abreu, R. K., Díaz Romero, N., Villalba, L. Caracterización clínica y epidemiológica de los suicidios en Montevideo y de los intentos de autoeliminación (IAE) en el Hospital de Clínicas en el período abril 2000-abril 2001: el método de la autopsia psicológica; Clinical features and epidemiology of suicides in Montevideo and suicide attempts at the Hospital de Clinicas from april 2000 to april 2001. Rev. Psiquiatr. Uruguay, 2003; 67(1): 5-20.

Ludwig, B., Dwivedi, Y., 2018. The concept of violent suicide, its underlying trait and

neurobiology: A critical perspective. Eur. Neuropsychopharmacol. 28(2), 243-251. http://doi:10.1016/j.euroneuro.2017.12.001.

Lundin A, Lundberg I, Hallsten L. (2010). Unemployment and mortality-A longitudinal prospective study on selection and causation in 49321 Swedish middle-aged men. *Journal of Epidemiology and Community Health* 64: 22-28

Luo F, Florence C, Quispe-Agnoli M, Ouyang L, Crosby A. (2011). Impact of Business Cycles on US Suicide Rates, 1928-2007. *American Journal of Public Health* 101(6), 1139-1146.

MacDonald M, Murphy T R. (1990). *Sleepless Souls: suicide in early modern England*. Oxford University Press: Oxford.

MacDonald M. (1995). Suicidal behavior- social section. In: Berrios and Porter eds, *A history of clinical psychiatry*. Athlone Press: London.

Madu, S. N., Matla, M. P. The prevalence of suicidal behaviours among secondary school adolescents in the Limpopo Province, South Africa. S. Afr. J. .Psychol., 2003; 133: 126-32.

Maes, M., Cosyns, P., Meltzer, H.Y., De Meyer, F., Peeters, D., 1993. Seasonality in violent suicide but not in nonviolent suicide or homicide. Am. J. Psychiatry. 150(9), 1380-1385.

Makris, G.D., Reutfors, J., Larsson, R., Isacsson, G., Ösby, U., Ekbom, A., Ekselius, L., Papadopou, F.C., 2016. Serotonergic medication enhances the association between suicide and sunshine. J. Affect. Disord. 189, 276-281. http://doi:10.1016/j.jad.2015.09.056

Malone, K. M., Szanto K., Corbitt, E. M., Mann, J. J. Clinical assessment versus research methods in the assessment of suicidal behavior. Am J Psychiatry, 1995; 152: 1601-7.

Maloney, E., Degenhardt, L., Darke, S., Mattick, R. P., Nelson, E. Suicidal behavior and associated risk factors among opioid- dependent individuals: a case- control study. Addiction, 2007; 102: 1033-41.

Mann J.J. , Currier D. M. Stress, genetics and Epigenetics effects in the neurobiology of suicidal behavior and depression. Eur Psychiatry, 2010; 25 (5): 268-71.

Mann JJ, Waternaux C, Haas GL, Malone KM. Toward a clinical model of suicidal behavior in psychiatric patients. Am J Psychiatry (1999) 156:181-9.

Mann, J. J. Neurobiology of suicidal behaviour. Nat Rev Neurosci, 2003; 4(10): 819-28.

Mann, J. J., Apter, A., Bertolote, J., Beautrais, A., Currier, D., Haas, A., et al. Suicide prevention strategies: a systematic review. JAMA., 2005; 294(16): 2064-74.

Mann, J. J., Arango, V. A., Avenevoli, S., Brent, D. A., Champagne, F. A., Clayton, P., et al. Candidate endophenotypes for genetic studies of suicidal behavior. Biol Psychiatry, 2009; 65(7): 556-63.

Mann, J. J., Ellis, S. P., Waternaux, C. M., Liu, X., Oquendo, M. A., Malone, K. M., et al. Classification trees distinguish suicide attempters in major psychiatric disorders: a model of clinical decision making. J. Clin. Psychiatry, 2008; 69(1): 23-31.

Manuck, S. B., Flory, J. D., Ferrell, R. E., Mann, J. J., Muldoon, M. F. A regulatory polymorphism of the monoamine oxidase-A gene may be associated with variability in aggression, impulsivity, and central nervous system serotonergic responsivity. Psychiatry Res., 2000; 96: 9-23.

Marazziti, D., Baroni, S., Pirone, A., Giannaccini, G., Betti, L., Testa, G., Schmid, L., Palego, L., Borsini, F., Bordi, F., Piano, I., Gargini, C., Castagna, M., Catena-Dell'Osso, M., Lucacchini, A., 2013. Serotonin receptor of type 6 (5-HT$_6$) in human prefrontal

cortex and hippocampus post-mortem: an immunohistochemical and immunofluorescence study. Neurochem. Int. 62(2), 182-188. http://doi:10.1016/j.neuint.2012.11.013.

Maris R W, Berman A, Silverman M. (2000). *Comprehensive Textbook of Suicidology.* The Guilford Press: New York

Maris, R. W. Suicide. Lancet, 2002; 360: 319–26.

Marsh I. (2010). *Suicide: Foucault, history and truth*. Cambridge University Press: Cambridge

Martin R, Barresi J. (2006). *Rise and fall of soul and self: an intellectual history of personal identity*. Columbia University Press: New York.

Martinotti, G., Mandelli, L., Di Nicola, M., Serretti, A., Fossati, A., Borroni, S., et al. Psychometric characteristic of the Italian version of the Temperament and Character Inventory—Revised, personality, psychopathology, and attachment styles. Compr. Psychiatry, 2008; 49(5): 514-22.

Maruani, J., Anderson, G., Lejoyeux, B.E.M., Bellivier, F., Geoffroy, P.A., 2018. The neurobiology of adaptation to seasons: Relevance and correlations in bipolar disorders. Chronobiol. Int. [Epub ahead of print]. http://doi:10.1080/07420528.2018.1487975.

Matsubayashi, T., Sawada, Y., & Ueda, M., 2013. Does the installation of blue lights on train platforms prevent suicide? A before-and-after observational study from Japan. J Aff. Disord, 147(1-3), 385-388

Matsubayashi, T., Sawada, Y., & Ueda, M., 2014. Does the installation of blue Lights on train platforms shift suicide to another station?: Evidence from Japan. J Aff. Disord, 169, 57-60.

Mboussou, M., Milebou-Aubusson, L. Suicides and attempted suicides at the Jeanne Ebori Foundation, Libreville (Gabon)]. Med. Trop. (Mars), 1989; 49(3): 259-67.

McCauley, M., Russell, V., Bedford, D., Khan, A., Kelly, R. Assessment following deliberate self-harm: who are we seeing and are we following the guidelines? Ir. J. Psych. Med., 2001; 18: 116-9.

McGirr, A., Renaud, J., Bureau, A., Seguin, M., Lesage, A., Turecki, G. Impulsive-aggressive behaviours and completed suicide across the life cycle: a predisposition for younger age of suicide. Psychol. Med., 2008; 38(3): 407-17.

McGirr, A., Turecki, G. The relationship of impulsive aggressiveness to suicidality and other depression-linked behaviors. Curr. Psychiatry Rep., 2007; 9(6): 460-66.

McKenzie, K., van Os, J., Samele, C., Van Horn, E., Tattan, T., Murray, R. Suicide and attempted suicide among people of Caribbean Origin with psychosis living in the UK. Br. J. Psychiatry, 2003; 183: 40-4.

Melhem, N. M., Brent, D. A., Ziegler, M., Iyengar, S., Kolko, D., Oquendo, M., et al. Familial pathways to early-onset suicidal behavior: familial and individual antecedents of suicidal behavior. Am. J. Psychiatry., 2007; 164(9): 1364-70.

Meltzer H.Y. Treatment of suicidality in schizophrenia. Ann .N Y. Acad. Sc., 2001; 932:44–58.

Meltzer, D. (1976). The delusion of clarity of insight. Int. J. Psycho-Anal., 57(1-2), 141-150.

Meng, D., Li, H.Q., Deisseroth, K., Leutgeb, S., Spitzer, N.C., 2018. Neuronal activity regulates neurotransmitter switching in the adult brain following light-induced stress. Proc. Natl. Acad. Sci. USA. 115(20), 5064-5071. http://doi:10.1073/pnas.1801598115

Messaoud A, Mensi R, Mrad A, Mhalla A, Azizi I, Amemou B, et al. Is low total cholesterol levels associated with suicide attempt in depressive patients? Ann Gen Psychiatry (2017) 16:20. https://doi:10.1186/s12991-017-0144-4.

Mikami, K., Inomata, S., Hayakawa, N., Ohnishi, Y., Enseki, Y., Ohya, A., et al. Frequency and clinical features of pervasive developmental disorder in adolescent suicide attempts. Gen. Hosp. Psychiatry, 2009; 31: 163–6.

Miller M, Azrael D, Hemenway D. The epidemiology of case fatality rates for suicide in the northeast. Ann Emerg Med. (2004) 43:723-30.

Min, J.Y., Min, K.B., 2018. Outdoor light at night and the prevalence of depressive symptoms and suicidal behaviors: a cross- sectional study in a nationally representative sample of Korean adults. J. Affect. Disord. 227, 199-205. http://doi.10.1016/j.jad.2017.10.039

Ministry of Health. Suicide Facts: 2010 data. Ministry of health, Wellington, retrieved online: www.health.govt.nz/publication/suicide-facts-deaths-and-intentional-self-harm-hospitalisations-2010.

Miret, M., Nuevo, R., Morant, C., Sainz-Cortón, E., Jiménez-Arriero, M. Á., López-Ibor, J. J., et al. Quality of written information about suicide attempts. Rev. Psiquiatr. Salud Mental, 2010; 3(1): 13-8.

Mirkovic, B., Labelle, R., Guilé, J.M., Belloncle, V., Bodeau, N., Knafo, A., Condat, A., Bapt-Cazalets, N., Marguet, C., Breton, J.J., Cohen, D., Gérardin, P., 2015. Coping skills among adolescent suicide attempters: results of a multisite study. Can. J. Psychiatry. 60(2 Suppl 1), S37-45.

Mitsui, N., Nakai, Y., Inoue, T., Udo, N., Kitagawa, K., Wakatsuki, Y., Kameyama, R., Toyomaki, A., Ito, Y.M., Kitaichi, Y., Nakagawa, S., Kusumi, I., 2017. Association between suicide-related ideations and affective temperaments in the Japanese general adult population. PLoS One. 12(6), e0179952.

Molnar, B. E., Berkman, L. F., Buka, S. L. Psychopathology, childhood sexual abuse and other childhood adversities: relative links to subsequent suicidal behaviour in the US. Psychol. Med., 2001; 31: 965–77.

Monnin, J., Thiemard, E., Vandel, P., Nicolier, M., Tio, G., Courtet, P., et al. Sociodemographic and psychopathological risk factors in repeated suicide attempts: Gender differences in a prospective study. J. Affect. Disord., 2012;136(1): 35-43.

Morrisey S K. (2006). *Suicide and the body politics in Imperial Russia*. Cambridge University Press: Cambridge.

Mortier, P., Auerbach, R.P., Alonso, J., Axinn, W.G., Cuijpers, P., Ebert, D.D., ... & Nock, M.K. 2018b. Suicidal thoughts and behaviors among college students and same-aged peers: results from the World Health Organization World Mental Health Surveys. Soc. Psychiatry. Psychiatr.Epidemiol. 53(3), 279-288.

Mortier, P., Auerbach, R.P., Alonso, J., Bantjes, J., Benjet, C., Cuijpers, P., ... & O'Neill, S. 2018a. Suicidal thoughts and behaviors among first-year college students: Results from the WMH-ICS Project. J. Am. Acad. Child. Adolesc. Psychiatry. 57(4), 263-273.

Mrazek, P. J., Haggerty, R. J. (Eds.) Reducing the risk for mental disorder: Frontiers for prevention intervention research. Washington, DC: National Academy Press, Institute of Medicine 1994.

Muldoon MF, Manuck SB, Matthews KA. Lowering cholesterol concentrations and mortality: a quantitative review of primary prevention trials. BMJ. (1990) 301:309-14.

Muneer, A., 2017. Mixed States in Bipolar Disorder: Etiology, Pathogenesis and Treatment. Chonnam. Med. J. 53, 1-13. http://doi:10.4068/cmj.2017.53.1.1.

Murray A. (1998). *Suicide in the Middle Ages, vol. I, The violent against themselves*. Oxford University Press: Oxford.

Nagoshi, E., Sugino, K., Kula, E., Okazaki, E., Tachibana, T., Nelson, S., Rosbash, M.,

2010. Dissecting differential gene expression within the circadian neuronal circuit of Drosophila. Nat. Neurosci. 13(1), 60-68. http://doi:10.1038/nn.2451

Neumayer E. (2004). Recessions lower (some) mortality rates: evidence from Germany. *Social science and medicine* 58(6), 1037-1047.

Nishi, D., Matsuoka, Y., Kawase, E., Nakajima, S., Kim, Y. Mental health service requirements in a Japanese medical centre emergency department. Emerg. Med. J., 2006; 23(6): 468-69.

Nordentoft, M, Sogaard, M. Registration, psychiatric evaluation and adherence to psychiatric treatment after suicide attempt. Nord. J. Psychiatry, 2005; 59: 213-6.

Nordström, P., Samuelsson, M., Åsberg, M. Survival analysis of suicide risk after attempted suicide. Acta Psychiatr. Scand., 1995; 91(5): 336-40.

Norström T, Grönqvist H. (2015). The Great Recession, unemployment and suicide. *Journal of epidemiology and community health* 69(2), 110-116.

Nwosu, S. O., Odesanmi, W. O. Pattern of suicides in Ile-Ife, Nigeria. West Afr. J. Med,. 2001; 20: 259-62.

O'Carroll, P. W. Attempted suicide among young adults: progress toward a meaningful estimate of prevalence. Am. J. Psychiatry,1992; 149: 41-55.

O'Neill, S., McLafferty, M., Ennis, E., Lapsley, C., Bjourson, T., Armour, C., Murphy, S., Bunting, B., Murray, E., Socio-demographic, mental health and childhood adversity risk factors for self-harm and suicidal behaviour in College students in Northern Ireland. J. Affect. Disord. 239, 58-65. http://doi:10.1016/j.jad.2018.06.006

O'Shaughnessy, E. (1981). A Clinical Study of a Defensive Organization. Int. J. Psycho-Anal., 62:359-369.

O'Shaughnessy, E. (1986). A 31/2-year-old boy's melancholic identification with an

original object. Int. J. Psycho-Anal., 67: 173-179.

O'Shaughnessy, E. (1992). Enclaves and Excursions. Int. J. Psycho-Anal., 73:603-611

O'Carroll, P. W., Berman, A. L., Maris, R. W., Moscicki, E. K., Tanney, B. L., Silverman, M. M. Beyond the Tower of Babel A nomenclature for suicidology. Suicide Life Threat. Behav, 1996; 26: 237–52.

Odejide, A. O., Williams, A. O., Ohaeri, J. U., Ikuesan, B. A. The epidemiology of deliberate self-harm. The Ibadan experience. Br. J. Psychiatry, 1986; 149: 734-37.

Ogden, T. H. (2004). The analytic third: Implications for psychoanalytic theory and technique. Psychoanal. Q., 73(1), 167-195.

Okasha, A., Lotaif, F. Attempted suicide. An Egyptian investigation. Acta Psychiatr. Scand., 1979; 60(1): 69-75.

Oquendo MA, Sullivan GM, Sudol K, Baca-Garcia E, Stanley BH, Sublette ME, et al. Toward a biosignature for suicide. Am J Psychiatry (2014) 171: 1259-77. https://doi:10.1176/appi.ajp.2014.14020194.

Oquendo, M. A., Bongiovi-Garcia, M. E., Galfalvy, H., Goldberg, P. H., Grunebaum, M. F., Burke, A. K., et al. Sex differences in clinical predictors of suicidal acts after major depression: a prospective study. Am. J. Psychiatry, 2007; 164:134–41.

Oquendo, M. A., Galfalvy, H., Russo, S., Ellis, S. P., Grunebaum, M. F., Burke, A., Mann, J. J. Prospective study of clinical predictors of suicidal acts after a major depressive episode in patients with major depressive disorder or bipolar disorder. Am. J. Psychiatry, 2004; 161(8): 1433-41.

Oquendo, M. A., Placidi, G. P., Malone, K. M., Campbell, C., Keilp, J., Brodsky, B., et al. Positron emission tomography of regional brain metabolic responses to a

serotonergic challenge and lethality of suicide attempts in major depression. Arch. Gen. Psychiatry, 2003; 60(1): 14-23.

Ösby, U., Brandt, L., Correia, N., Ekbom, A., Sparén, P. Excess mortality in bipolar and unipolar disorder in Sweden. Arch. Gen. Psychiatry 2001; 58:844–50.

Osváth, P., Kelemen, G., Erdös, M. B., Vörös, V., Fekete, S. The main factors of repetition: review of some results of the Pecs Center in the WHO/ EURO Multicentre Study on Suicidal Behaviour. Crisis, 2003; 24: 151–154.

Ovuga, E., Boardman, J., Wasserman, D. Integrating mental health into primary health care: local initiatives from Uganda. World Psychiatry, 2007; 6(1): 60-71.

Owens, D., Horrocks, J., House, A. Fatal and non-fatal repetition of self-harm. Systematic review. Br. J. Psychiatry, 2002; 181: 193–99.

Pandey, G. N., Dwivedi, Y., Rizavi, H. S., Teppen, T., Gaszner, G. L., Roberts, R. C., Conley, R. R. GSK-3β gene expression in human postmortem brain: regional distribution, effects of age and suicide. Neurochem. Res., 2009; 34(2): 274-85.

Pandey, G. N., Ren, X., Rizavi, H. S., Conley, R. R., Roberts, R. C., Dwivedi, Y. Brain-derived neurotrophic factor and tyrosine kinase B receptor signalling in post-mortem brain of teenage suicide victims. Int. J. Neuropsychopharmacology., 2008; 11(8): 1047-53.

Panek, M., Pietras, T., Witusik, A., Wieteska, Ł., Małachowska, B., Mokros, Ł., Fendler, W., Szemraj, J., Kuna, P., 2015. Identification and association of relationships between selected personal and environmental factors and formal components of temperament and strategies of coping with stress in asthmatic patients. Physiol. Behav. 149, 269-278.

Patel, S., Batterham, P.J., Calear, A.L., Cryer, R., 2016. Predictors of Comfort and Confidence among medical students in providing care to patients at risk of suicide. Acad. Psychiatry. 40(6), 919-922.

Paul K, Moser K. (2009). Unemployment impairs mental health: meta-analyses. *Journal of Vocational Behavior* 74: 264–82.

Pawlak J, Dmitrzak-Weglarz M, Wilkosc M, Szczepankiewicz A, Leszczynska-Rodziewicz A, Zaremba D, et al. Suicide behavior as a quantitative trait and its genetic background. J Affect Disord. (2016) 206:241-50. https://doi:10.1016/j.jad.2016.07.029.

Pawlak, J., Szczepankiewicz, A., Kapelski, P., Rajewska-Rager, A., Slopien, A., Skibinska, M., Czerski, P., Hauser, J., Dmitrzak-Weglarz, M., 2017. Suicidal behavior in the context of disrupted rhythmicity in bipolar disorder-Complementary research of clock genes with suicide risks factors and course of disease. Psychiatry. Res. 257, 446-449. http://doi:10.1016/j.psychres.2017.07.057.

Pelser, D. J. W., Oberholzer, D. J. Attempted suicide (parasuicide), Medunsa/Ga-Rankuwa Hospital, South Africa. 1987; 14: 22-4.

Peng, R., Dai, W., Li, Y., 2018. Low serum free thyroxine level is correlated with lipid profile in depressive patients with suicide attempt. Psychiatry. Res. 266, 111-115. http://doi:10.1016/j.psychres.2018.05.059.

Perera S, Eisen RB, Bhatt M, Dennis BB, Bawor M, El-Sheikh W, et al. Exploring metabolic factors and health behaviors in relation to suicide attempts: A case-control study. J Affect Disord. (2018) 229:386-95. https://doi:10.1016/j.jad.2017.12.060.

Pierce A. (1967). The Economic cycle and the social suicide rate. *American Sociological Review* 32 (3), 457- 462.

Pirkis, J. E., Burgess, P. M., Meadows, G. N., Dunt, D. R. Suicidal ideation and suicide attempts as predictors of mental health service use. Med. J. Austr., 2001; 175(10): 542-5.

Pirkis, J., Beautrais, A., Durkee, T. Suicide attempts in New Zealand and Australia. In: Wassermann D., Wassermann C. ed., Oxford Textbook of Suicidology and Suicide Prevention. Oxford: Oxford University Press 2009.

Placidi, G. P., Oquendo, M. A., Malone, K. M., Huang, Y. Y., Ellis, S. P., Mann, J. J. Aggressivity, suicide attempts, and depression: relationship to cerebrospinal fluid monoamine metabolite levels. Biol. Psychiatry, 2001; 50: 783-91.

Polyzos N. (2012). Health and the financial crisis in Greece Health and the financial crisis in Greece. *Lancet* 379(9820), 1000-1011.

Pompili M, Innamorati M, Vichi M, Masocco M, Vanacore N, Lester D, Serafini G, Tatarelli R, De Leo D Girardi P. (2011). Inequalities and impact of socioeconomic-cultural factors in suicide rates across Italy. *Crisis* 32(4), 178-185.

Pompili M, Longo L, Dominici G, Serafini G, Lamis DA, Sarris J, et al. Polyunsaturated fatty acids and suicide risk in mood disorders: A systematic review. Progr NeuroPsychopharmacol Biol Psychiatry (2017) 74:43-56. https://doi:10.1016/j.pnpbp.2016.11.007.

Pompili, M. Exploring the phenomenology of suicide. Suicide Life Threat. Behav., 2010; 40: 234–44.

Pompili, M., Forte, A., Palermo, M., Stefani, H., Lamis, D.A., Serafini, G., et al. Suicide risk in multiple sclerosis: a systematic review of current literature. J. Psychosom. Res., 2012a; 73(6): 411-7.

Pompili, M., Girardi, P., Tatarelli, R., Iliceto, P., De Pisa, E., Tondo, L., Akiskal, K.K., Akiskal, H.S., 2008. TEMPS-A (Rome): psychometric validation of affective temperaments in clinically well subjects in mid- and south Italy. J. Affect. Disord. 107(1-3), 63-75.

Pompili, M., Goracci, A., Giordano, G., Erbuto, D., Girardi, P., Klonsky, E. D., &

Baldessarini, R. J., (2015). Relationship of non-suicidal self-injury and suicide attempt: a psychopathological perspective. J Psychopathology 21, 348-353

Pompili, M., Iliceto, P., Luciano, D., Innamorati, M., Serafini, G., Del Casale, A., et al. Higher hopelessness and suicide risk predict lower self-deception among psychiatric patients and non-clinical individuals. Riv. Psichiatr., 2011b; 46(1): 24-30.

Pompili, M., Innamorati, M., Gonda, X., Serafini, G., Sarno, S., Erbuto, D., Palermo, M., Elena Serretti, M., Stefani, H., Lester, D., Perugi, G., Akiskal, H., Siracusano, A., Rihmer, Z., Tatarelli, R., Amore, M., Girardi, P., 2013. Affective temperaments and hopelessness as predictors of health and social functioning in mood disorder patients: a prospective follow-up study. J. Affect. Disord. 150(2), 216-222.

Pompili, M., Innamorati, M., Gonda, X., Serafini, G., Sarno, S., Erbuto, D., et al. Affective temperaments and hopelessness as predictors of health and social functioning in mood disorder patients: a prospective follow-up study. J. Affect. Disord., 2013; 150(2): 216-22.

Pompili, M., Innamorati, M., Rihmer, Z., Gonda, X., Serafini, G., Akiskal, H., Amore, M., Niolu, C., Sher, L., Tatarelli, R., Perugi, G., Girardi, P. 2012. Cyclothymic-depressive-anxious temperament pattern is related to suicide risk in 346 patients with major mood disorders. J. Affect. Disord. 136, 405-411.

Pompili, M., Innamorati, M., Szanto, K., Di Vittorio, C., Conwell, Y., Lester, D., Tatarelli, R., Girardi, P., Amore, M., 2011. Life events as precipitants of suicide attempts among first-time suicide attempters, repeaters, and non-attempters. Psychiatry. Res. 186(2-3), 300-305

Pompili, M., Innamorati, M., Szanto, K., Di Vittorio, C., Conwell, Y., Lester, D., et al. Life events as precipitants of suicide attempts among first-time suicide attempters, repeaters, and non-attempters. Psychiatry Res., 2011a; 186: 300–5.

Pompili, M., Serafini, G., Di Cosimo, D., Dominici, G., Innamorati, M., Lester, D., et al. Psychiatric comorbidity and suicide risk in patients with chronic migraine. Neuropsychiatr. Dis. Treat., 2010; 6: 81-91.

Pompili, M., Tatarelli, R. Evidence-based practice in Suicidology. Gottingen: Hoegrefe 2010.

Pompili, M., Venturini, P., Campi, S., Seretti, M. E., Montebovi, F., Lamis, D. A., et al. Do stroke patients have an increased risk of developing suicidal ideation or dying by suicide? An overview of the current literature. CNS Neurosci. Ther., 2012b; 18(9): 711-21.

Posner, K., Brown, G. K., Stanley, B., Brent, D. A., Yershova, K. V., Oquendo, M. A., et al. The Columbia–Suicide Severity Rating Scale: initial validity and internal consistency findings from three multisite studies with adolescents and adults. Am. J. Psychiatry, 2011; 168(12): 1266-1277.

Post, R.M., Transduction of psychosocial stress into the neurobiology of recurrent affective disorder. Am. J. Psychiatry,1992; 149 (5): 999–1010.

Potter, D.M., Skene, D.J., Arendt, J., Cade, J.E., Grant, P.J., Hardie, L.J., 2016. Circadian Rhythm and Sleep Disruption: Causes, Metabolic Consequences, and Countermeasures. Endocr. Rev. 37(6), 584-608.

Preti A, Miotto P. (2005). Suicide in classical mythology: cues for prevention. *Acta Psychiatrica Scandinavica* 111, 384–391.

Preti, A., Miotto, P., 1998. Seasonality in suicides: the influence of suicide method, gender and age on suicide distribution in Italy. Psychiatry. Res. 81, 219-231.

Qi, X., Hu, W., Mengersen, K., Tong, S., 2014. Socio-environmental drivers and suicide in Australia: Bayesian spatial analysis. BMC. Public. Health. 14, 681.

http://doi:10.1186/1471-2458-14-681.

Rabinow P, Rose N. (2003). *The Essential Foucault*. The New York Press: New York.

Ramberg, I. L. Promoting suicide prevention. An evaluation of a program for training trainers in psychiatric clinical work. Doctoral Thesis, Karolinska Instituet, Stockholm 2003.

Ramberg, I. L., Wasserman, D. Prevalence of reported suicidal behaviour in the general population and mental health-care staff. Psychol. Med, 2000; 30(5): 1189-96.

Rancāns, E., Lapiņš, J., Renberg, E. S., Jacobsson, L. Self-reported suicidal and help seeking behaviours in the general population in Latvia. Soc. Psychiatry Psychiatr. Epidemiol., 2003; 38(1): 18-26.

 Reppermund, S., Ising, M., Lucae, S., Zihl, J. Cognitive impairment in unipolar depression is persistent and non-specific: further evidence for the final common pathway disorder hypothesis. Psychol. Med., 2009; 39(4): 603-14.

Rey, H. (1979). Schizoid phenomena in the borderline. In: Bott- Spillius E., 1988, Melanie Klein Today, Vol. I. London: Routledge. Pp. 203-229.

Rey, H. (1988). That which patients bring to analysis. Int. J. Psycho-Anal., 69: 457 - 470.

Rey, H. (1994). Universals of Psychoanalysis in the Treatment of Psychotic and Borderline States. London: Free Association Press.

Rihmer, Z. Suicide risk in mood disorders. Curr. Opin. Psychiatry, 2007; 20: 17–22.

Rihmer, Z., Gonda, X., Torzsa, P., Kalabay, L., Akiskal, H.S., Eory, A., 2013. Affective temperament, history of suicide attempt and family history of suicide in general practice patients. J. Affect. Disord. 149(1-3), 350-354.

Robinson, J., Harris, M. G., Harrigan, S. M., Henry, L. P., Farrelly, S., Prosser, A., et al. Suicide attempt in first-episode psychosis: a 7.4-year follow-up study. Schizophr. Res, 2010; 116: 1–8.

Robson, B., Purdie, G., Cram, F., Simmonds, S. Age standardisation–an indigenous standard?. Emerg. Themes Epidemiol., 2007; 4(1): 3-15.

Rogers, J.R., DeShon, R.P., 1992. A reliability investigation of the eight clinical scales of the suicide opinion questionnaire. Suicide. Life-Threat. Behav. 22, 428-441.

Rosen G. (1971). History in the study of suicide. *Psychological Medicine* 1, 267-85.

Rotenstein, L.S., Ramos, M.A., Torre, M., Segal, J.B., Peluso, M.J., Guille, C., Sen, S., Mata, D.A., 2016. Prevalence of Depression, Depressive Symptoms, and Suicidal Ideation Among Medical Students: A Systematic Review and Meta-Analysis. JAMA. 316(21), 2214-2236.

Roy, A. Characteristics of opiate dependent patients who attempt suicide. J. Clin. Psychiatry, 2002; 63: 403-7.

Roy, A. Features associated with suicide attempts in depression: a partial replication. J. Affect. Disord., 2003; 27: 35–8.

Rudd, M. D. Suicidality in clinical practice: Anxieties and answers. J. Clin. Psychol., 2006; 62(2): 157-9.

Rumble, M.E., Dickson, D., McCall, W.V., Krystal, A.D.K., Case, D., Rosenquist, P.B., Benca, R.M., 2018. The Relationship of Person-Specific Eveningness Chronotype, Greater Seasonality, and Less Rhythmicity to Suicidal Behavior: A Literature Review. J. Affect. Disord. 227, 721-730. https://doi:10.1016/j.jad.2017.11.078

Sawa, M., Koishikawa, H., Osaki, Y., 2017. Risk Factors of a Suicide Reattempt by Seasonality and the Method of a Previous Suicide Attempt: A Cohort Study in a

Japanese Primary Care Hospital. Suicide. Life. Threat. Behav. 47(6), 688-695. http://doi:10.1111/sltb.12326.

Schlebusch L., Burrows S. Suicide attempts in Africa. In: Wassermann D., Wassermann C. ed , Oxford Textbook of Suicidology and Suicide Prevention. Oxford: Oxford University Press 2009

Schlebusch, L. Suicidal behaviour in South Africa. Pietermaritzburg, University of KwaZulu-Natal Press 2005.

Schmidtke, A., Bille- Brahe, U., De Leo, D. Suicidal behavior in Europe: results from the WHO/ EURO multicenter study on suicidal behavior. Goettingen: Hoegrefe and Huber 2001.

Schmidtke, A., Bille-Brahe, U., DeLeo, D., Kerkhof, A., Bjerke, T., Crepet, P., et al. Attempted suicides in Europe: rates trends and sociodemographic characteristics of suicide attempters during the period 1989- 1992. Results of the WHO/EURO Multicentre study on parasuicide. Acta Psychiatr. Scand., 1996; 93: 127-338.

Schneider, B., Schnabel, A., Wetterling, T., Bartusch, B., Weber, B., Georgi, K. How do personality disorders modify suicide risk?. J. Pers. Disord., 2008; 22(3): 233-45.

Schrijvers DL, Bollen J, Sabbe BG. The gender paradox in suicidal behavior and its impact on the suicidal process. J Affect Disord. (2012) 138:19-26. https://doi:10.1016/j.jad.2011.03.050.

Seabourne A, Seabourne G. (2001). Suicide or accident – self-killing in medieval England: series of 198 cases from the Eyre records. *British Journal of Psychiatry* 178, 42-47.

Searles, H. F. (1959). The effort to drive the other person crazy—an element in the aetiology and psychotherapy of schizophrenia. 32(1), 1-18.

Segal, H. (1993). On the clinical usefulness of the concept of death instinct. Int. J. Psycho-Anal., 74(1): 55-61.

Segoviano-Mendoza M, Cárdenas-de la Cruz M, Salas-Pacheco J, Vázquez-Alaniz F, La Llave-León O, Castellanos-Juárez F, et al. Hypocholesterolemia is an independent risk factor for depression disorder and suicide attempt in Northern Mexican population. BMC Psychiatry (2018) 18:7. https://doi:10.1186/s12888-018-1596-z.

Serafini, G., Adavastro, G., Canepa, G., Capobianco, L., Conigliaro, C., Pittaluga, F., Murri, M.B., Valchera, A., De Berardis, D., Pompili, M., Lindqvist, D., Brundin, L., Amore, M., 2017. Abnormalities in Kynurenine Pathway Metabolism in Treatment-Resistant Depression and Suicidality: A Systematic Review. CNS. Neurol. Disord. Drug. Targets. 16(4), 440-453. http://doi:10.2174/1871527316666170413110605

Serafini, G., Pompili, M., Innamorati, M., Fusar-Poli, P., Akiskal, H.S., Rihmer, Z., Lester, D., Romano, A., de Oliveira, I.R., Strusi, L., Ferracuti, S., Girardi, P., Tatarelli, R., 2010. Affective temperamental profiles are associated with white matter hyperintensity and suicidal risk in patients with mood disorders. J. Affect. Disord. 129, 47-55.

Seregi, B., Kapitány, B., Maróti-Agóts, Á., Rihmer, Z., Gonda, X., Döme, P., 2017. Weak associations between the daily number of suicide cases and amount of daily sunlight. Prog. Neuropsychopharmacol. Biol. Psychiatry. 73, 41-48. http://doi:10.1016/j.pnpbp.2016.10.003.

Shneidman E S. (1993). Commentary: Suicide as psychache. *Journal of nervous and mental disease* 181(3), 145-147.

Shneidman E S. (2001). *Comprehending Suicide Landmarks in 20th-Century Suicidology*. American Psychological Association: Washingtion.

Shneidman E S., (1985) *Definition of Suicide*. John Wiley and Sons: New York.

Shneidman ES. The suicidal mind. NewYork, NY: Oxford University Press, (1996). 133 p.

Silverman, M.M., Berman, A.L., Sanddal, N.D., O'Carroll, P.W., Joiner, T.E., 2007. Rebuilding the tower of Babel: a revised nomenclature for the study of suicide and suicidal behaviors. Part 1: Background, rationale, and methodology. Suicide. Life. Threat. Behav. 37(3), 248-263.

Silverman, M.M., Berman, A.L., Sanddal, N.D., O'carroll, P.W., Joiner, T.E., 2007a. Rebuilding the tower of Babel: a revised nomenclature for the study of suicide and suicidal behaviors. Part 1: Background, rationale, and methodology. Suicide Life Threat Behav. 37(3), 248-263.

Silverman, M.M., Berman, A.L., Sanddal, N.D., O'Carroll, P.W., Joiner, T.E., 2007b. Rebuilding the tower of Babel: a revised nomenclature for the study of suicide and suicidal behaviors. Part 2: suicide-related ideations, communications and behaviors. Suicide Life Threat Behav. 37(3), 264-277.

Solano P, Pizzorno E, Gallina A M, Mattei C, Gabrielli F, Kayman J (2012). Employment status, inflation and suicidal behavior: An analysis of a stratified sample in Italy. *International Journal of Social Psychiatry* 58 (5): 471-484.

Stack S. (2000). Suicide: A 15-Year Review of the Sociological Literature Part I: Cultural and Economic Factors. *Suicide and Life-Threat Behavior* 30: 145–162.

Stanford SM, Bottini M, Bottini N. The role of LMPTP in the metabolic syndrome. In: Bence KK, editor. Protein tyrosine phosphatase control of metabolism. New York, NY, Heidelberg, Dordrecht, London: Springer; (2015). p. 203-20.

Strozier R M (2002). *Foucault, subjectivity, and identity: historical constructions of subject and self*. Wayne State University Press: Detroit.

Stuckler D, Basu S, Suhrcke M, Coutts A, McKee M. (2009). The public health effect of economic crises and alternative policy responses in Europe: an empirical analysis. *Lancet* 374, 315–23.

Stuckler D, Basu S, Suhrcke M, Coutts A, McKee M. (2011). Effects of the 2008 recession on health: a first look at European data. *Lancet* 378(9786), 124-125.

Sudol K, Mann JJ. Biomarkers of suicide attempt behavior: towards a biological model of risk. Curr Psychiatry Rep. (2017) 19(6):31. https://doi:10.1007/s11920-017-0781-y.

Sun, J., Guo, X., Ma, J., Zhang, J., Jia, C., Xu, A., 2011. Seasonality of suicide in Shandong China, 1991-2009: associations with gender, age, area and methods of suicide. J. Affect. Disord. 135(1-3), 258-266. http://doi:10.1016/j.jad.2011.08.008.

Tanabe, S., Terao, T., Shiotsuki, I., Kanehisa, M., Ishii, K., Shigemitsu, O., Fujiki, M., Hoaki, N., 2016. Anxious temperament as a risk factor of suicide attempt. Compr. Psychiatry. 68, 72-77.

Taylor C. (1989). *Sources of the self: the making of the modern identity*. Harvard University Press: Cambridge MA.

Tondo, L., Vasquez, G.H., Sani, G., Pinna, M., Baldessarini, R.J., 2018. Association of suicidal risk with ratings of affective temperaments. J. Affect. Disord. 229, 322-327.

Toro, K., Dunay, G., Bartholy, J., Pongracz, R., Kis, Z., Keller, E., 2009. Relationship between suicidal cases and meteorological conditions. J. Forensic. Leg. Med. 16(5), 277-279. http://doi:10.1016/j.jflm.2008.12.015.

Tosini, G., Ferguson, I., & Tsubota, K., 2016. Effects of blue light on the circadian system and eye physiology. Molecular vision, 22, 61-72.

Tosini, G., Ye, K., Iuvone, P.M., 2012. N-acetylserotonin: neuroprotection, neurogenesis, and the sleepy brain. Neuroscientist. 18(6), 645-653. http://doi:10.1177/1073858412446634.

Trakhtenbrot, R., Gvion, Y., Levi-Belz, Y., Horesh, N., Fischel, T., Weiser, M., et al.

2016. Predictive value of psychological characteristics and suicide history on medical lethality of suicide attempts: A follow-up study of hospitalized patients. J. Affect. Disord. 199, 73-80. http://doi:10.1016/j.jad.2016.03.054

Turecki, G., Brent, D.A., 2016. Suicide and suicidal behaviour. Lancet. 387(10024), 1227-1239.

Valtonen, H., Suominen, K., Partonen, T., Ostamo, A., Lönnqvist, J., 2006. Time patterns of attempted suicide. J. Affect. Disord. 90, 201-207.

Van Houwelingen, C.A., Beersma, D.G., 2001. Seasonal changes in 24-h patterns of suicide rates: a study on train suicides in the Netherlands. J. Affect. Disord. 66, 215-223.

Van Houwelingen, C.A., Kerkhof, A.J., Beersma, D.G., 2010. Train suicides in the Netherlands. J. Affect. Disord. 127, 281-286. http://doi:10.1016/j.jad.2010.06.005.

Vaughan, C.H., Shrestha, Y.B., Bartness, T.J., 2011. Characterization of a novel melanocortin receptor-containing node in the SNS outflow circuitry to brown adipose tissue involved in thermogenesis. Brain. Res. 1411, 17-27. http://doi:10.1016/j.brainres.2011.07.003.

Vázquez, G.H., Gonda, X., Lolich, M., Tondo, L., Baldessarini, R.J., 2018. Suicidal Risk and Affective Temperaments, Evaluated with the TEMPS-A Scale: A Systematic Review. Harv. Rev. Psychiatry. 26(1), 8-18.

Veisani, Y., Delpisheh, A., Sayehmiri, K., Moradi, G., Hassanzadeh, J., 2017. Seasonality in Violent and Nonviolent Methods of Suicide Attempts: A Cross-Sectional Study on Systematic Registry Data. Acta. Med. Iran. 55(8), 507-513.

Veisani, Y., Delpisheh, A., Sayehmiri, K., Moradi, G., Hassanzadeh, J., 2018. Trends of Suicide Attempts and Completed Suicide in Ilam Province of Iran; A Demographic Analysis Study. Bull. Emerg. Trauma. 6(3), 245-248. http://doi:10.29252/beat-0603010.

Vevera J, Zukov I, Morcinek T, Papezova H. Cholesterol concentrations in violent and non-violent women suicide attempters. Eur Psychiatry (2003) 18:23-7.

Vyssoki, B., Kapusta, N.D., Praschak-Rieder, N., Dorffner, G., Willeit, M., 2014. Direct effect of sunshine on suicide. JAMA. Psychiatry. 71, 1231-1237. http://doi:10.1001/jamapsychiatry.2014.1198

Vyssoki, B., Praschak-Rieder, N., Sonneck, G., Blüml, V., Willeit, M., Kasper, S., Kapusta, N.D., 2012. Effects of sunshine on suicide rates. Compr. Psychiatry. 53(5),535-539. http://doi:10.1016/j.comppsych.2011.06.003.

Wallin, U., Runeson, B., 2003. Attitudes towards suicide and suicidal patients among medical students. Eur. Psychiatry. 18(7), 329-333.

White, R.A., Azrael, D., Papadopoulos, F.C., Lambert, G.W., Miller, M., 2015. Does suicide have a stronger association with seasonality than sunlight? BMJ. Open. 5, e007403. http://doi:10.1136/bmjopen-2014-007403.

Widlocher, D. (2003). Introduction. In: Leuzinger-Bohleber M., Dreher A.U., Canestri J., Pluralism and Unity?: Methods of Research in Psychoanalysis. New York: The International Psychoanalysis Library

Willour VL, Seifuddin F, Mahon PB, Jancic D, Pirooznia M, Steele J, et al. A genome-wide association study of attempted suicide. Mol Psychiatry (2012) 17:433-44. https://doi:10.1038/mp.2011.4.

Winnicott, D. W. (1971). Playing and Reality. London: Tavistock.

Winnicott,, D. W. (1953). Transitional Objects and Transitional Phenomena - A Study of the First Not-Me Possession. Int. J. Psycho-Anal., 34:89-97

Winnicott,, D. W. (1954). Metapsychological and clinical aspects of regression within the psycho-analytical set-up. In Collected papers: Through paediatrics to psychoanalysis (pp. 278-294). London: Tavistock, 1958.

Winslow B. (1840). The anatomy of suicide. Henry Renshaw ed.: London.

Woo, J.M., Okusaga, O., Postolache, T.T., 2012. Seasonality of Suicidal Behavior. Int. J. Environ. Res. Public. Health. 9(2), 531-547. http://doi:10.3390/ijerph9020531.

Woodhead, E.L., Cronkite, R.C., Moos, R.H., Timko, C., 2014. Coping strategies predictive of adverse outcomes among community adults. J. Clin. Psychol. 70(12), 1183-1195.

World Health Organization. Global Burden of Disease (GBD), (2017).

World Health Organization. Preventing Suicide: a Global Imperative. Geneva, (2014).

World Health Statistics 2017: Monitoring health for the SDGs http://apps.who.int/gho/data/node.sdg.3-4-viz-2?lang=en

Wu S, Ding Y, Wu F, Xie G, Hou J, Mao P. Serum lipid levels and suicidality: a meta-analysis of 65 epidemiological studies. J Psychiatry Neurosci. (2016) 41:56-69.

Wu YW, Su YJ, Chen CK. Clinical characteristics, precipitating stressors, and correlates of lethality among suicide attempters. Chang Gung Med J. (2009) 32(5):543-52.

Yur'yev A, Värnik A, Värnik P, Sisask M, Leppik L. (2012) Role of social welfare in European suicide prevention. *International Journal of Social Welfare* 21(1): 26-33.

Zimmerman S L. (1987a). States' public welfare expenditures as predictors of state suicide rates. *Suicide and Life Threatening Behaviors* 17(4):271-87.

Zimmerman S L. (1987b) State-level public policy as a predictor of individual and family well-being. *Women Health* 12(3-4):161-88.

Zimmerman S L. (1990) The connection between macro and micro levels: states' spending for hospitals and their suicide rates. *Suicide and Life Threatening Behaviors* 20(1):31-55.

Zimmerman S L. (2002) States' spending for public welfare and their suicide rates, 1960 to 1995: what is the problem*? Journal of Nervous and Mental Disease* 190(6):349-60.