

GENDER-SPECIFIC RISK FACTORS FOR SUICIDE
IN MAJOR DEPRESSIVE DISORDER

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DEDICATION

To Ana-Maria, Adrian, Adrian and Alex.

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Contribution of authors

Chapter 2 consists in the text of the following manuscript:

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The first author of the case control study, Ioana M. Dalca, organized the data, cleaned the data and scored it, performed the statistical analysis, interpreted the results and wrote the manuscript. Gustavo Turecki, the senior author, supervised the project and was involved in the project at each of these steps, designed the study, and obtained funding and ethics approval. Alexander McGirr, a co-author of the manuscript, contributed to the funding application, the design of the study and data collection. Johanne Renaud, the second co-author of the manuscript, contributed in the planning of the study.

TABLE OF CONTENTS

| | |
|--|-----------|
| DEDICATION..... | 2 |
| Contribution of authors..... | 4 |
| TABLE OF CONTENTS..... | 5 |
| LIST OF TABLES..... | 6 |
| ABSTRACT..... | 7 |
| Chapter 1 BACKGROUND LITERATURE..... | 9 |
| AND OBJECTIVES..... | 9 |
| 1.1 Gender and Suicide..... | 11 |
| 1.1.1 Gender and Suicide Completion..... | 11 |
| 1.1.2 Gender & Suicide Attempts..... | 11 |
| 1.2 Suicide and Risk Factors..... | 13 |
| 1.2.1 Suicide and Depression..... | 13 |
| 1.2.2 Suicide and Other Risk Factors..... | 14 |
| 1.2.3 Suicide and Personality..... | 16 |
| 1.3 Gender and Suicide Risk..... | 17 |
| 1.3.1 Explaining the Gender Paradox..... | 17 |
| 1.3.2 Gender & Depression..... | 19 |
| 1.3.3 Gender & Personality..... | 20 |
| 1.4 Preface to Chapter 2: Research Objectives..... | 23 |
| Chapter 2 A CASE CONTROL STUDY..... | 26 |
| 2.1 Introduction..... | 27 |
| 2.2 Methods..... | 30 |
| 2.2.1 Participants..... | 30 |
| 2.2.2 Diagnostic Assessments..... | 31 |
| 2.2.3 Personality Trait Assessments..... | 34 |
| 2.2.4 Statistical Analysis..... | 36 |
| 2.3 Results..... | 39 |
| 2.3.1 Suicide Effects..... | 39 |
| 2.3.2 Effects after Stratification by Gender..... | 45 |
| 2.3.5 Multiple Variable Analysis..... | 54 |
| 2.4 Discussion..... | 55 |
| Chapter 3 SUMMARY AND DISCUSSION..... | 64 |
| Chapter 4 CONCLUSION..... | 86 |
| BIBLIOGRAPHY..... | 88 |

LIST OF TABLES

| | |
|---|----|
| Table 1: Personal History Results – The Overall Sample..... | 40 |
| Table 2: Psychopathology Results – The Overall Sample..... | 42 |
| Table 3: Personality and Behavioural Predispositions Results – The Overall Sample | 44 |
| Table 4: Personal History Results – Subsample of Men | 45 |
| Table 5: Personal History Results – Subsample of Women | 46 |
| Table 6: Psychopathology Results – Subsample of Men | 47 |
| Table 7: Psychopathology Results – Subsample of Women | 49 |
| Table 8: Personality and Behavioural Predispositions Results – Subsample of Men | 51 |
| Table 9: Personality and Behavioural Predispositions Results – Subsample of Women..... | 52 |
| Table 10: Interaction effects resulting from the two-way analysis of variance..... | 53 |

ABSTRACT

Gender differences in suicidal behaviour entail a challenging paradox: more women attempt suicide than men, while more men commit suicide than women. The majority of suicide victims have a history of major depressive disorder (MDD), though only a small minority of those suffering from MDD will die by suicide. The present study aimed to explore the moderating role of gender in suicide completion, with particular focus on personality predispositions, Axis I and II psychopathology, while controlling for the effect of MDD. In the context of a case-control design, 201 suicide completers (160 men and 41 women) and 129 living controls (90 men and 39 women) with a history of MDD were recruited in Montreal, Canada. Participants were evaluated via the psychological autopsy method. Differences were found between men and women in the significant risk factors, suggesting that psychopathology and predispositions related to impulsivity-aggressivity and impulse-dyscontrol may have different relative contributions to suicide in depressed men and women.

ABRÉGÉ

Les différences dans le comportement suicidaire entre les hommes et les femmes, un paradoxe: Plus de femmes que d'hommes font des tentatives de suicide bien que plus d'hommes que de femmes les réussissent. La majorité des victimes du suicide ont des antécédents de trouble de dépression majeur (MDD), même si seulement une faible minorité des personnes atteintes de MDD vont mettre fin à leurs jours. La présente étude entend relativiser l'importance du genre chez les personnes qui se sont suicidées en mettant l'accent plus particulièrement sur les prédispositions propres à chaque individu, la psychopathologie de l'axe I et II, en contrôlant les effets du MDD. Les cas présentés, 201 suicides (160 hommes et 41 femmes) et 129 tentatives de suicide (90 hommes et 39 femmes) ont été recrutés à Montréal, Canada. Les participants ont été évalués selon la méthode de l'autopsie psychologique. En ce qui a trait aux facteurs de risque, des différences ont été notées entre les hommes et les femmes, ce qui laisse entendre que la psychopathologie et les prédispositions relatives à l'impulsivité-agressivité ainsi qu'au non-contrôle-impulsif peuvent avoir contribué différemment au suicide chez les hommes et les femmes en dépression.

**Chapter 1 BACKGROUND LITERATURE
AND OBJECTIVES**

If men and women differ in their psychological health throughout life, they certainly do in the behaviour that brings death upon the self – suicide. Suicide ranks among the top ten causes of death for individuals of all ages and is the leading cause of death in most developed countries for those younger than 35 years, particularly among men (Diekstra, 1993; Mao, Hasselback, Davies, Nichol, & Wigle, 1990)(Statistics Canada, 1997). As such, suicide has now become the leading cause of unnecessary and premature death (Maris, Berman, & Silverman, 2000). In Quebec alone, there are between 1,200 and 1,500 completed suicides per year, approximately half of which have a history of major depressive disorder (MDD). While depression is the fourth leading cause of disease burden in the world and first in the Americas (Üstün, Ayuso-Mateos, Chatterji, Mathers, & Murray, 2004), its most severe complication is undeniably suicide completion. The lifetime mortality risk by suicide in depressed individuals remains low, somewhere between 7 to 15% (Angst, Stassen, Clayton, & Angst, 1999, 2002; Guze & Robins, 1970) and accordingly, the majority of patients with MDD do not die by suicide. Why some patients commit suicide while others do not is a question that has long puzzled both researchers and clinicians. Given the suggestion that individuals may have a certain diathesis to suicide, studies have consequently focused on personality traits as determinants of an increased risk for suicide. In addition, substantial evidence suggests that these factors may have a different relative contribution to suicide, and moreover, that gender may in fact moderate their effects. The present master's

project aims to investigate the risk factors for suicide in major depression, with a particular focus on predisposing factors that may have a different effect according to gender.

1.1 Gender and Suicide

1.1.1 Gender and Suicide Completion

Across the world, the rate of completed suicides is higher for men than for women, with China being the only clearly documented exception (Phillips, 2002; Phillips, Li, & Zhang, 2002). Also, several international epidemiological and autopsy studies have found a male-to-female ratio that is greater than one which remains consistent across all age groups (WHO, 1996) with a range between 2.8 and 5.7 in US, Canadian, Australian, and Scandinavian samples (Brent, Johnson, Bartle, Bridge, & et al., 1993; Desjarlais, Eisenberg, Good, & Kleinman, 1995; Diekstra, 1993; Gould, Fisher, Parides, Flory, & Shaffer, 1996; Grøholt, Ekeberg, Wichstrom, & Haldorsen, 1997; Holinger, Offer, Barter, & Bell, 1994; Marttunen, Aro, Henriksson, & Lonnqvist, 1991) (WHO, 2000; Statistics Norway, 1994).

1.1.2 Gender & Suicide Attempts

On the other hand, the prevalence of suicide attempts has been estimated around 4.2% among women and 1.5% among men (Moscicki, 1994). Indeed, as reported consistently in epidemiological studies on the general population; self-reported suicide attempts; in-patients admitted for suicide attempts; and inmates, women attempt suicide up to two-to-three times more often than men across most

nations (Canetto & Sakinofsky, 1998; Daigle & Cote, 2006; King, 1997; Roy, 2000; Roy & Janal, 2005; Weissman, et al., 1999; Wichstrøm & Rossow, 2002).

Concordantly, the average male-to-female ratio of patients hospitalized for nonfatal suicidal behaviour across different sites in the WHO/EURO Multicentre Study has been observed to be about 1:1.66, without any significant variation (Bille-Brahe, et al., 1997). However, a few noteworthy exceptions of equal and slightly more men than women among attempters have been reported in Helsinki (Ostamo & Lonnqvist, 2001) and among New York City Puerto Rican patients (Fernandez-Pol, 1986) respectively. Moreover, the female preponderance has also been confirmed in non-Western samples for suicide attempts (Aghanwa, 2004; Khan & Reza, 1998), and for suicidal ideation (Garrison, Addy, Jackson, McKeown, & et al., 1991; Lewinsohn, Rohde, & Seeley, 1996).

Albeit in different directions, the fact that gender is a major risk factor for both suicide attempts and suicide completion clearly describes the gender paradox of suicide. Understanding the role of gender in suicidal behaviour may thus be crucial towards improving sensitivity and specificity in predicting its most fatal outcome. While several complementary explanations for the gender discrepancies have been put forth in the literature (Canetto & Sakinofsky, 1998; Hawton, 2000; Lester, 1996; Lewinsohn, Rohde, Seeley, & Baldwin, 2001; Maris, et al., 2000; Moscicki, 1994; Murphy, 1998; Qin, Agerbo, Westergaard-Nielson, Eriksson, & Mortensen, 2000; Wannan & Fombonne, 1998), the insufficient apprehension of the

gender paradox still remains an important obstacle in preventing suicide completion.

1.2 Suicide and Risk Factors

1.2.1 Suicide and Depression

Preceding their death, the majority of suicide completers have experienced at least one diagnosable mental disorder (Leenars, et al., 1998; Lesage, et al., 1994). Psychopathology, most often present in the form of major depression, is perhaps the most important predictor of suicidal behaviours including ideation, attempt, and completion (Bhatia, Aggarwal, & Aggarwal, 2000). While depression is the fourth leading cause of disease burden in the world and first in the Americas (Üstün, et al., 2004), its most severe complication is undoubtedly suicide completion. To be sure, the diagnostic criteria for major depression may have been met by a large number of suicide completers (Isometsa, Aro, Henriksson, Heikkinen, & Lonnqvist, 1994; Isometsa, Henriksson, et al., 1994) and could include up to half of Canadian male completers (Kim, et al., 2003; Lesage, et al., 1994). However, since the mortality risk by suicide in depressed individuals remains relatively low, somewhere between 7 to 15% (Angst, et al., 1999, 2002; Blair-West, Mellsop, & Eyeson-Annan, 1997; Guze & Robins, 1970), delineating the role of risk factors for suicide beyond depression is crucial if we are to develop a specific model of suicide completion.

1.2.2 Suicide and Other Risk Factors

The risk for suicide is clearly multifactorial: adverse childhood experiences, childhood exposure to traumatic events and history of early abuse (Davidson, Hughes, George, & Blazer, 1996; Leenars, et al., 1998; Molnar, Berkman, & Buka, 2001; Molnar, Buka, & Kessler, 2001; Nelson, et al., 2002; Paolucci, Genuis, & Violato, 2001; Santa Mina & Gallop, 1998), and familial transmission of suicidal behaviour and sexual abuse (Brent, et al., 2002; Roy, 2000; Runeson & Asberg, 2003) all contribute significantly to increasing the risk for attempted suicide. Such risk is also increased by substance dependence, whether alcohol or other psychoactive drugs as well as by demographic characteristics such as unemployment, never having married and limited access to necessary treatments (Leenars, et al., 1998). Age is an even more important risk factor for suicidal behaviour, since in almost all industrialized regions suicide rates increase with age (McIntosh, 1992) and peak among the elderly for both genders (Girard, 1993). In contrast, patterns in developing areas show that suicide rates peak between 15 and 59 for men, and 15 to 29 for women (Girard, 1993). Furthermore, age determines variation in the association between psychiatric disorders and suicide, such that the rate of comorbidity with personality disorders is significantly higher among youth suicides compared to older suicides, even after controlling for axis I psychopathology (Dumais, Lesage, Alda, et al., 2005).

Medically serious suicide attempts are self-destructive acts causing serious physical harm which require medical hospitalization (Elliott, Pages, Russo, Wilson, & Roy-Byrne, 1996). Naturally, the methods associated with them are highly violent and usually lethal; such as firearms, hanging or jumping from heights. These types of attempts have long been considered a key risk for subsequent suicide attempts and completion (Isometsa & Lonnqvist, 1998; Ivarsson, Larsson, & Gillberg, 1998; Krupinski, et al., 1998; Osvath, Voros, & Fekete, 2004). Underscoring its importance, efforts have already been made to create neural network models for detecting medically serious suicide attempts in patients (Modai, Kuperman, Goldberg, Goldish, & Mendel, 2004). While medically serious suicide attempts are often fatal, a history of nonfatal suicide attempts increase the rate of completed suicide 100-fold (Suokas, Suominen, Isometsä, Ostamo, & Lönnqvist, 2001).

Risk factors for suicide among patients with MDD include experience with previous suicide attempts, demographic variables, clinical symptomatology (such as hopelessness and comorbidity), discharge from psychiatric inpatient care, psychosocial risk factors (such as history of sexual or physical trauma), and seasonal effects (Barraclough & Pallis, 1975; Beck, Brown, Berchick, Stewart, & et al., 1990; Beck, Brown, & Steer, 1989; Beck, Steer, Kovacs, & Garrison, 1985; Beck, Steer, & Trexler, 1989; Beck & Weishaar, 1990; Brent, et al., 2002; Cheng, Chen, Chen, & Jenkins, 2000; Fawcett, et al., 1990; Goldacre, Seagroatt, & Hawton, 1993; Gould, et al., 1996; Kim, et al., 2003). Other studies have suggested that individuals may have

a certain diathesis for suicide, and that suicidal behaviour occurs when several risk factors interact. This may be conceptualized as the trigger-threshold model for suicide (J. J. Mann, Waternaux, Haas, & Malone, 1999) (J. J. Mann, 1998) where risk factors could be organized into the trigger domain (including clinical characteristics such as acute illness, adverse life events and so on), and the threshold domain (including biological predisposition and personality variants) (J. J. Mann, 1998; J. J. Mann, et al., 1999). With the aim of improving suicide prediction beyond that provided by the presence of depression, it might be indispensable to focus on factors encompassing the threshold domain such as personality correlates.

1.2.3 Suicide and Personality

Personality characteristics, as reflected in behavioural traits and personality disorders, represent significant determinants of increased risk for suicide. The prevalence of personality disorders has been evaluated in recent large-scale surveys to be quite high: 9% in community samples in the USA (Samuels, et al., 2002) and 13% in Norway (Torgersen, Kringlen, & Cramer, 2001). On the other hand, among Canadian men who have completed suicide, a higher frequency of individuals - thirty per cent - meet the criteria for borderline or antisocial personality disorders, or both (Kim, et al., 2003). Furthermore, individuals diagnosed with antisocial personality disorder score high on measures of aggression, especially overt aggression (Jaffe, Hurley, & Wolfe, 1990), and in turn, high hostility ratings are associated with suicidal behaviour. Moreover, not only does comorbidity with cluster B traits,

impulsive-aggressive behaviours and substance use disorders differentiate between suicide completers and living control participants (Kim, et al., 2003; Lesage, et al., 1994), but such personality variants also increase susceptibility to suicide attempts (Corruble, Damy, & Guelfi, 1999; Malone, Szanto, Corbitt, & Mann, 1995; Pendse, Westrin, & Engstrom, 1999; Soloff, Lis, Kelly, Cornelius, & et al., 1994; Stein, Apter, Ratzoni, Har-Even, & Avidan, 1998; Windle, 1994). Finally, higher levels of impulsive/aggressive behaviours are present among suicide completers versus controls also in the presence of major depression, and independently from comorbidity with substance abuse disorders (Dumais, Lesage, Alda, et al., 2005; Kim, et al., 2003). This suggests that impulsive/aggressive behaviours combined with behavioural disinhibition and facilitated by substance use disorders, may mediate suicide in major depression.

1.3 Gender and Suicide Risk

1.3.1 Explaining the Gender Paradox

Several theories have been put forth to explain the gender differences in suicidal behaviour. For example, validity of the data on suicide attempts has been put under question, and it has been suggested that underreporting of nonfatal suicidal behaviour in men and overestimation of women's suicide attempt rates relative to men's, may result from gender differences in response sets (Canetto & Sakinofsky, 1998) and differential sampling of women and men due to reliance on hospital data (Whitehead, Johnson, & Ferrence, 1973). Nonetheless, it seems clear

that an artefact of data is unlikely to explain the gender paradox in suicide (Canetto & Sakinofsky, 1998). Others have suggested that differential socialization of men and women is also a contributor (Nolen-Hoeksema & Girgus, 1994; Webster-Stratton, 1996) such that traditional masculinity increases psychological vulnerability among men and promotes maladaptive coping strategies (Moller-Leimkuhler, 2003). Conversely, nonfatal suicidal behaviour is conceived as an appropriate coping strategy for women (Canetto & Sakinofsky, 1998). Such factors lead the two genders to employ different suicide attempt methods, to employ the same method differently, and to stage their suicidal behaviour differently (Canetto, 1997; Canetto & Sakinofsky, 1998).

Regardless of social antecedents, the lethality of the method employed by men to attempt suicide is higher than that of women in the Western world (Rich, Ricketts, Fowler, & Young, 1988). It has been argued that if only medically serious suicide attempts are taken into account, the gender difference in suicide attempts disappears (Beautrais, 2002). This result is in line with the notion that on average, women attempters have less suicidal intent (Haw, Hawton, Houston, & Townsend, 2003; Rich, et al., 1988) and that rates of nonfatal suicidal acts are comparable among women and men when controlling for instrumental behaviour (Daigle & Cote, 2006). However, others have speculated that the difference in method lethality among genders can hardly explain why women report more suicide attempts, since

only a minority of suicide attempts have a fatal outcome (Wichstrøm & Rossow, 2002).

On the other hand, a prospective cross-sectional study of a representative sample of 12 to 20 year-old Norwegian students in a two year follow up, highlighted no gender difference in suicide attempts when previous attempts, depressed mood, physical appearance, perceived pubertal timing and romantic involvement were controlled for (Wichstrøm & Rossow, 2002); further suggesting that the gender differences in this age group may be better explained by women's higher exposure to several risk factors compared to men. Whether gender differences in suicidal behaviour are due to differential exposure to known risk factors or other factors inseparable from gender is not yet clearly established (Hawton, 2000). Nevertheless, it would seem that it is the mediating and moderating effects of gender on several risk factors that may considerably explain the gender paradox, and in effect, improve specificity in predicting suicide.

1.3.2 Gender & Depression

Beyond several demographic and psychosocial factors (Canetto & Sakinofsky, 1998; Hawton, 2000; Lester, 1996; Lewinsohn, et al., 2001; Moscicki, 1994; Murphy, 1998; Wannan & Fombonne, 1998), there is growing evidence supporting the idea that risk factors play a different role in increasing predisposition to suicide in males and females, and as such, each gender may have a different suicide diathesis. For instance, it has been suggested that women's higher rates of

depression (Moscicki, 1994) and negative attribution style (Jack, 1992) may explain why women engage in more nonfatal suicidal behaviour; although it does not explain why women perform fatal suicidal acts less often (Canetto & Sakinofsky, 1998). However, the different diathesis among genders in relation to depression may be supported by the observation that female suicides suffer in a significantly higher proportion from major depression than male suicides (Arsenault-Lapierre, Kim, & Turecki, 2004; Brent, Baugher, Bridge, Chen, & Chiappetta, 1999). Studies investigating gender differences in the onset of depression have suggested that women are more sensitive to stress (Nazroo, Edwards, & Brown, 1997; Piccinelli & Wilkinson, 2000) despite the fact that women do not have higher rates of adverse life events. Yet, they do seem to react more intensely to these events and seem to have a closer association between the life event and the onset of depression (Piccinelli & Wilkinson, 2000). Moreover, females seem to be more sensitive to the effect of adverse childhood events, including sexual abuse (Veijola, et al., 1998). As a risk factor for eventual suicide attempts, history of sexual or physical trauma is particularly present in depressed women (Brent, et al., 2002).

1.3.3 Gender & Personality

Nevertheless, completed suicide rates are consistently higher in men than in women (Diekstra, 1993)(WHO, 2000) independent of the effect of depression or affective disorders. Some have suggested that the risk for suicide in women including depression and other forms of internalizing behaviours may be overridden

in men by increased lethal intentions, impulsivity, aggression, alcohol abuse and disruptive behaviours that put men at greater overall risk for suicide completion (Wichstrøm & Rossow, 2002). In reference to impulsive-aggression-related risk in men, investigations into the prevalence of Axis II psychopathology show higher rates among men than women in studies where the community sample displays a large proportion of antisocial personality disorder (ASPD) (i. e. 3% (Samuels, et al., 2002)), and an equal distribution among genders when the prevalence of ASPD is low (i.e. 1.3% in Oslo community sample; (Torgersen, et al., 2001)). ASPD, the most common of all personality disorders according to epidemiologic studies conducted before 1990, displays a rate of approximately 2-3% in the general population with a prevalence rate in men that is five-fold that in women (Weissman, 1993). As of 2000, the prevalence is approximately 3% in men and 1% in women (APA, 2000). This gender gap has also been observed among the homeless where DSM-III-R ASPD rates are between 23- 25% in men and 7-10% in women (North & Smith, 1993). Moreover, among college students, men score higher on the aggressiveness trait (measured with the Buss-Perry Aggression Questionnaire) than women (Harris & Knight-Bohnhoff, 1996). Gender differences are thus observed in both disorder and trait descriptors of impulsive-aggression associated aspects of personality in the general population.

Although there has been little empirical investigation comparing men and women suicide completers while controlling for axis I psychopathology and gender-

specific behavioural norms, available studies found direct or indirect evidence suggesting that male suicide is more strongly associated to conditions related to impulsive-aggressivity (Gould, et al., 1996; Rich, et al., 1988; Shaffer, et al., 1996). Among suicide completers, women are more likely to suffer from major depression disorder while men are more likely to meet criteria for substance, personality and childhood disorders (Arsenault-Lapierre, et al., 2004). In addition, among youth suicides, men are more likely to have conduct/antisocial disorders than women (Brent, et al., 1999; Marttunen, et al., 1995; Rich, et al., 1988). However, because these studies have been carried out only in adolescent suicide, and did not control for the presence of axis-I psychopathology, they are of limited generalizability. In addition, it should also be noted that the finding that men consistently use more violent and lethal suicide attempt methods, which correlate with lifetime history of aggression (Beautrais, 2002; Canetto & Sakinofsky, 1998; Dumais, Lesage, Lalovic, et al., 2005; Hawton, 2000; Maris, et al., 2000), also supports the hypothesis that male suicides have higher levels of impulsive-aggressive behaviours. Thus, these traits could account for a different diathesis between the genders, at least in part.

1.4 Preface to Chapter 2: Research Objectives

In order to advance the general efforts of identifying susceptibility factors for completed suicide, this thesis aimed to investigate the role of gender in suicide. This goal was approached via a case-control study. More specifically, this study set out to identify gender-specific risk factors for suicide, while controlling for the effect of major depression. It was hypothesized that gender moderates the impact of suicide risk factors. In other words, while affected by a similar psychopathological condition, namely major depressive disorder (MDD), risk factors for suicide would have a different relative contribution in men and women. Moreover, we hypothesized that conditions related to impulsive-aggressivity would be relatively higher among depressed men who have completed suicide, even after controlling for psychopathology.

In view of our discussion of personality deviations, both dimensional and categorical assessments were chosen for this study. Aggressivity was operationalised as recalled aggressive behaviour and as the hostility trait (encompassing several dimensions of aggressivity, including both direct and indirect forms of hostility). These were expected to be related to suicide completion, especially among men, given previous reports (Dumais, Lesage, Alda, et al., 2005), and the fact that they theoretically tap on overlapping constructs. To account for impulsive-aggressivity, we also explored impulsivity as a risk factor. Given that suicide completer men are more impulsive than suicide completer women (McGirr, et al., 2006), and that very

highly impulsive individuals have been shown to have higher odds for suicide completion (Dumais, Lesage, Alda, et al., 2005), we expected that high levels of this trait would increase the odds for suicide completion among men in our study.

To expand on the concept of personality, and as an alternative to more traditional conceptualisations, the dimensional approach of temperaments and characters was chosen, as well. It was expected that temperaments related to impulsive-aggressivity would most likely show dissociation between suicide completers and control participants. Thus, novelty seeking, given its overlap in concept with impulsiveness, and marginal association with suicide among depressed men (Dumais, Lesage, Alda, et al., 2005), was thought to potentially give similar results to impulsivity. Reward dependence, given its higher predominance among suicidal women (McGirr, et al., 2006), was expected to display significant results among women, or at least an effect on suicide completion that would be moderated by gender. We hypothesised that persistence would not significantly increase odds for suicide completion, given that the trait would be inhibitory of impulsive acts, though the possibility exists that such a trait would be contributory in the fatality of a planned suicidal act. While harm-avoidance, cooperativeness and self-transcendence were not expected to significantly affect suicide completion odds, neither among women, nor men, it was thought that self-directedness could have more severe outcomes in a depressive state among men, given this dimension's

contrast to the apathy, anhedonia, difficulty concentrating and hopelessness/helplessness, which might be symptomatic in a depressive episode.

With regard to categorical aspects of personality, axis II diagnoses were considered appropriate. In particular, Cluster B diagnoses were considered most relevant towards the impulsive-aggressive hypothesis, and thus expected to differentiate between suicide completer men and depressed controls. Similarly, among axis I psychopathology categories, it was expected that those related to impulse-dyscontrol - alcohol dependence, drug dependence, gambling – would all dissociate between suicide completers and their counterparts, especially among men.

Chapter 2 A CASE CONTROL STUDY

This chapter consists in the text of the following manuscript:

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2.1 Introduction

Across all age groups in Western societies, men consistently complete suicide at a higher rate than women (Diekstra, 1993), and frequently do so three-to-six times more often than women in US, Canadian, Australian and Scandinavian samples (Brent, et al., 1993; Desjarlais, et al., 1995; Diekstra, 1989, 1993; Gould, et al., 1996; Grøholt, et al., 1997; Holinger, et al., 1994; Marttunen, et al., 1991)(Statistics Norway, 1994; WHO, 2000). However, suicide attempts have for the most part been reported to be up to two-to-three times more frequent among women from the general population and hospitals in both Western and non-Western settings (Aghanwa, 2004; Canetto & Sakinofsky, 1998; Daigle & Cote, 2006; Diekstra, 1993; Khan & Reza, 1998; King, 1997; Roy, 2000; Roy & Janal, 2005; Weissman, et al., 1999; Wichstrøm & Rossow, 2002) compared to men. Plainly, the fact that gender is a major risk factor for both suicide completion and suicide attempts, albeit in different directions, clearly illustrates what is referred to as the gender paradox of suicide.

The majority of suicide victims have a history of at least one diagnosable mental disorder preceding their death (Leenars, et al., 1998; Lesage, et al., 1994), most commonly major depressive disorder (MDD) (Angst, et al., 2002; Arseneault-Lapierre, et al., 2004; Isometsa, Aro, et al., 1994; Isometsa, Henriksson, et al., 1994; Kim, et al., 2003; Lesage, et al., 1994). As it is only a minority of individuals diagnosed with MDD that die by suicide (Angst, et al., 1999, 2002; Blair-West,

Cantor, Mellsop, & Eyeson-Annan, 1999; Blair-West, et al., 1997; Guze & Robins, 1970), delineating the psychological characteristics of depressed individuals that increase risk of suicide has been of great interest to researchers and clinicians alike. Irrespective of gender, risk factors for suicide among those suffering from MDD include experience with previous suicide attempts, demographic variables, clinical symptomatology, discharge from psychiatric inpatient care, psychosocial risk factors, as well as personality variants such as impulsive-aggressive traits (Barraclough & Pallis, 1975; Beck, et al., 1990; Beck, Brown, et al., 1989; Beck, et al., 1985; Brent, et al., 2002; Cheng, et al., 2000; Dumais, Lesage, Alda, et al., 2005; Fawcett, et al., 1990; Goldacre, et al., 1993; Gould, et al., 1996; Kim, et al., 2003; Lesage, et al., 1994; J. J. Mann, 1998; J. J. Mann, et al., 1999; Roy, 1983).

Underreporting of suicide attempts in men and over-reliance on hospital data (Canetto & Sakinofsky, 1998; Weissman, 1974; Whitehead, et al., 1973), differential sampling (Weissman, 1974; Whitehead, et al., 1973), socialization between genders (Nolen-Hoeksema & Girgus, 1994; Webster-Stratton, 1996) and suicidal intent (Haw, et al., 2003; Rich, et al., 1988) have all been brought forth to explain the discrepancy between women and men's suicidal behaviour. In fact, growing evidence suggests that risk factors may play a different role in male and female suicide, with each gender potentially having a different suicide diathesis. For instance, women may be more sensitive to the effect of adverse childhood events, including sexual abuse, on their experience with depression (Veijola, et al., 1998).

Whereas impulsive-aggressive traits, comorbidity with substance disorders, and developmental behavioural problems, already more prevalent among men according to epidemiological samples (Harris & Knight-Bohnhoff, 1996; North & Smith, 1993), may better account for men's higher rates of suicide. However, a number of previous studies investigating gender-specific risk factors for suicide have focused primarily on demographic characteristics and circumstances of death. As such, we overlook if established clinical and personality risk factors play a similar role in increasing predisposition to suicide in women as in men. Clearly, this is both a relevant clinical and scientific question. It is clinically relevant because suicide attempts are more frequent among women, and as a result, clinicians have to assess suicide risk in female patients more frequently. This question is also scientifically relevant because suicide completion is significantly more frequent among men, and consequently most of the studies on which clinical risk factors have been characterized and analyzed were based on samples composed primarily – if not exclusively - of male suicides. To our knowledge, no previous research has investigated gender-related suicide risk factors while controlling for axis-I psychopathology. This is an important problem in our view given that psychopathology may moderate the relationship between risk factors and suicide outcome, and is clearly differentially distributed between male and female suicides (Arsenault-Lapierre, et al., 2004).

Addressing the limitations of previous research, this study aimed to investigate gender effects on suicide risk in MDD (Skogman, Alsen, & Ojehagen, 2004; Suominen, Isometsa, Haukka, & Lonnqvist, 2004; Young, Fogg, Scheftner, & Fawcett, 1994). We report evidence which suggests that the gender moderation on the pathway to suicide completion is related to cluster B psychopathology, even after methodologically controlling for major depressive disorder.

2.2 Methods

2.2.1 Participants

We investigated a total sample composed of 330 participants, which included four different subgroups. The suicide cases were aged 17 to 82 years and included 160 men and 41 women who died by suicide and met the criteria for lifetime major depressive disorder (MDD). The controls were aged 19 to 73 years and included 90 men and 39 women recruited at psychiatric outpatient departments where they were currently being treated for recurrent major depressive disorder. These participants were selected to fulfill these criteria, from a unique database of suicide completers and outpatient control participants recruited by our group. The current analysis is therefore a secondary analysis of the database data.

The suicide sample was consecutively recruited and was representative of suicides in the general population with a history of major depressive disorder. Cases were identified at the Montréal Central Morgue, as part of a long-term collaboration with the Québec Coroner's Office. Written consent for participation

was obtained from the family of the deceased, and as described elsewhere (Dumais, Lesage, Alda, et al., 2005), family members were recruited to participate in psychological autopsies.

The control sample was recruited at psychiatric outpatient clinics of the Montréal area and consisted of individuals with a DSM-IV diagnosis of major depressive disorder, recruited for the absence of severe history of suicide attempts. After obtaining written consent from the subject, a best informant well acquainted with the participant was identified. In order to maximize comparability between groups, diagnostic and trait assessments for the controls were carried out in precisely the same manner as for the suicide cases. Participants were included in the sample if they were at least 17 years of age and presented with a lifetime history of major depressive disorder. However, participants were excluded if they met the criteria for bipolar disorder, schizophrenia, schizoaffective disorder or post-psychotic depressive disorder related to schizophrenia. The participation acceptance rate was $\geq 90\%$, and the demographic profile of those who refused to participate was similar to that of those who accepted. The project was approved by the local institutional review board, and the data was collected with written informed consent from both the informants and living participants.

2.2.2 Diagnostic Assessments

All psychiatric diagnoses were made using the psychological autopsy protocol for both the suicide cases and the control participants. The informants in our study

were most commonly a spouse or common-law partner (26%), a sibling (24%), a mother (19%) or a friend (10%).

Between July 1999 and December 2008, interviews were carried out by trained investigators who administered the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First, Spitzer, Gibbon, & Williams, 1997)(First, 2001) and the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II) (Gibbon, Spitzer, Williams, Benjamin, & First, 1997)(First, 1995). Reliability estimates using this procedure in our database were very good to excellent for most psychiatric disorders, specifically for MDD with kappa values were around 0.98 (Kim, et al., 2003; Lesage, et al., 1994). The estimates were substantial to outstanding (Landis & Koch, 1977) in our sample, for last 6-months and lifetime psychiatric disorders of both axes: 0.83 and 0.89 for MDD; 0.80 for alcohol dependence; 1.00 for drug dependence, 0.80 and 0.70 for anxiety disorders, 0.66 for generalised anxiety disorder; 1.00 for PTSD; and 1.00 for antisocial personality disorder. All diagnoses were assessed according to the Diagnostic and Statistical Manual of Mental Disorders 4th Edition (DSM-IV) (APA, 1994). The validity of this technique is clearly supported in the literature, and estimates of concordance between direct clinical assessment and by means of psychological autopsy have been shown to vary between 0.8 and 0.9 (Conner, Conwell, & Duberstein, 2001; Kelly & Mann, 1996). Our research group has already shown that SCID-I and II data is consistent across multiple respondents for the same

participant; that proxy-based interviews are consistent with the ones completed with participants themselves (Dumais, Lesage, Lalovic, et al., 2005; Dumais, Lesage, Alda, et al., 2005); and finally, that the rates of specific psychiatric diagnoses are not affected by the relationship of the informant to the suicide completer (Lesage, et al., 1994). The following diagnosis variables were used for the analyses: lifetime alcohol dependence, alcohol dependence in the last six months, lifetime non-alcohol substance dependence, drug substance dependence in the last six months, lifetime diagnoses for any anxiety disorder, any anxiety disorder in the last six months, eating disorder, psychotic symptomatology, antisocial personality disorder, borderline personality disorder, lifetime gambling, gambling in the last six months, Cluster A diagnosis, Cluster B diagnosis, Cluster C diagnosis, any axis II diagnosis, number of axis I diagnoses in the last six months, number of lifetime axis I diagnoses, and number of axis II diagnoses.

The semi-structured Mental Health Clinical Research Center Suicide History Form (MHCRC-SHF) (Oquendo, Halberstam, & Mann, 2003) was used to assess history of suicidal attempts. In total, 282 participants had complete information to establish whether a previous non-fatal suicide attempt was made, and 157 had information concerning the age of the first suicide attempt. Sociodemographic characteristics were assessed in a separate questionnaire. Childhood abuse was operationalised, with respect to incidence prior to the age of 18, with the item: “Has

(s)he ever been a victim of abuse by one or more people during the course of his or her life?”

2.2.3 Personality Trait Assessments

Using a variety of scales, psychopathological personality traits were assessed given our group’s previous experience with this procedure and demonstration of its excellent validity and interrater reliability (Dumais, Lesage, Alda, et al., 2005).

Lifetime aggression was assessed using the Brown-Goodwin Lifetime History of Aggression (BGLHA) (G. L. Brown, Goodwin, Ballenger, Goyer, & F., 1979), a 12-item interview schedule which assesses lifetime aggressive behaviour during childhood, adolescence and adulthood, with items such as “Has she had angry outbursts or temper tantrums in the past?” (Brown, et al., 1979). Both the total score and the adulthood score from the BGLHA were used in this study as measures of aggression. To further assess aggression, the Buss Durkee Hostility Inventory (BDHI), a self-report scale of 75 items (Buss & Durkee, 1957), was also used. The BDHI encompasses seven personality dimensions of hostility - assault, indirect hostility, irritability, negativity, resentment, suspicion and verbal hostility – and one of guilt. A sample indirect hostility item is “He sometimes spreads gossip about people he doesn't like” (Buss & Durkee, 1957).

The Barratt’s Impulsivity Scale (BIS-11) consisting of 30 self-report items covering attention, motor and nonplanning aspects of impulsivity (E. S. Barratt, 1959; E. S. Barratt, 1965; Patton, Stanford, & Barratt, 1995), was used to identify

highly impulsive participants (Barratt, et al., 1995). The total score from BIS-11 was used as a measure of impulsivity. The measure was also dichotomized into high (those with a score 75 or above), and low (those with a score below 75).

The Temperament and Character Inventory (TCI) (Cloninger, 1994), consisting in 239 items grouped in seven higher-order subscales and 25 lower-order subscales, was used to assess four basic temperaments and three characters. Novelty seeking, one of the temperaments, is a subscale encompassing exploratory excitability, impulsiveness, extravagance, or disorderliness, as exemplified by the item “X is slower than most people to get excited about new ideas and activities” (Cloninger, 1994). Harm avoidance, described by anticipatory worry, fear of uncertainty, shyness and fatigability is another temperament dimension, with a sample item of “Usually stays calm and secure in situations that most people would find physically dangerous” (Cloninger, 1994). A third temperament in the inventory, reward dependence, is reflected in items such as “Doesn't care very much whether other people like him/her or the way that (s)he does things” (Cloninger, 1994), and includes the subscales of sentimentality, openness to warm communication, attachment and dependence. The last temperament, persistence, is characterised by eagerness of effort, work hardenedness, ambitiousness, and perfectionism, and items such as “Is usually so determined that (s)he continues to work long after others have given up” (Cloninger, 1994).

One of three TCI character dimensions, self-directedness, consisted in items covering responsibility, purposefulness, resourcefulness, self-acceptance and enlightened second nature; one such item was “He spends most of his time doing things that seem necessary but not really important to him” (Cloninger, 1994). Cooperativeness, on the other hand, revolves around social acceptance, empathy, helpfulness, compassion, and pure-hearted conscience, with items like “Often considers another person's feelings as much as his/her own” (Cloninger, 1994). Finally, self-transcendence, a character described by self-forgetfulness, transpersonal identification and spiritual acceptance included items such as “He often feels a strong sense of unity with all the things around him” (Cloninger, 1994).

2.2.4 Statistical Analysis

Statistical data analysis was carried out with SPSS Statistical Package version 17.0 (SPSS Inc., Chicago). Unless otherwise specified, all tests were two-tailed and results with a critical value at $p < 0.05$ were considered significant.

For each categorical variable, we calculated the odds ratio (and 95% confidence intervals) of membership in the suicide completion group for those ‘with’ versus those ‘without’ the respective condition. The Pearson Chi-Square test was used for these comparisons and the one-tailed Fisher exact test was used for cases where at least one of the two-by-two table cell sizes was below 10. Analyses were first done for the entire sample, and then run separately for men and for women. To

test for homogeneity of odds ratios across genders, we used the Breslow-Day Chi-Square test, the Cochran Chi-Square test and the Mantel-Haentzel Chi-Square test.

For each continuous variable, the normality of distribution was assessed via normal probability and quantile plots, as well as indicators of skewness and kurtosis. All of the continuous variables that did not markedly deviate from normality were analyzed using a two-way analysis of variance with two independent factors (gender and suicide status) comprised of two levels each (man versus woman, suicide completer versus control). First, the main effects and the interaction between gender and suicide group were tested individually. Second, a full factorial model with the gender-group interaction, where gender and the group effects were considered simultaneous parameters, was tested (see Table 10). To investigate differences with respect to those variables that markedly deviated from normality (i.e. aggression, number of axis II diagnoses, cooperativeness, perseverance, and self-transcendence) we performed the following nonparametric tests: first the Mann-Whitney U-test (H. B. Mann & Whitney, 1947) and the two-sample Kolgomorov-Smirnov test (Smirnov, 1939) to assess differences between the two genders and between the two suicide status groups; and second, the Kruskal-Wallis test (Kruskal & Wallis, 1952) to rank the differences among the four gender-suicide status subgroups.

Multiple logistic regression analysis was carried out to adjust for covariates and assess the relationship between the major predictor variables. The outcome

variable was suicidal group (SC vs. CO) and the candidate parameters were the risk and vulnerability factors which expressed a significance value of $p < 0.20$ in the single variable and analysis of variance comparisons. Additionally, factors that had a strong theoretical basis for inclusion were also included. Next, the candidate variables were explored to minimize collinearity and correlation. Thus, we included the overarching variables (e.g. the Cluster B category rather than the borderline personality disorder, antisocial personality disorder, hostility, aggression or impulsivity scores) that still allowed for specificity in regards to impulsive-aggressive psychopathology (including both Cluster A and Cluster B categories rather than just the variable for the number of SCID II diagnoses). Candidate variables were included if their variance inflation factors were below 3.5. For all analyses, the female gender and the absence of the risk factor were designated as reference categories.

We constructed a model overarching different risk factors in order to control for the confounding effects among them. In the first block of candidate variables, we included the gender interaction with the variables in a forward stepwise manner. The variables that resulted from this modeling technique were selected for the next step if shown to be significant at $p < 0.10$. In the next block of the same candidate variables, we added all of the main effects of each variable in a forward stepwise manner. Similarly, the resulting variables were selected for the final model only if they were significant at $p < 0.10$. Finally, these variables were entered in one single

logistic model in order to obtain the corresponding estimates of significance and odds.

2.3 Results

2.3.1 Suicide Effects

2.3.1.1 Sociodemographic Characteristics and Personal History

The sample consisted of 160 men and 41 women who committed suicide, and 90 men and 39 women who did not, all of whom met the criteria for lifetime DSM-IV major depressive disorder. The mean age in these subgroups was 40.94 (s.d.=12.91), 41.83 (s.d.=12.66), 41.76 (s.d.=11.13) and 39.31 (s.d.=11.49), respectively. There were no differences between subgroups in age or gender distribution. The groups were also comparable with respect to civic status, education, ethno-cultural group and religion. Most of the participants, whether male or female, were originally from Quebec (95% and 91%) and were primarily Catholic (94% and 90%).

Depressed suicide completers had significantly higher odds than depressed controls for having a history of previous suicide attempts, though not for a history of childhood abuse (see Table 1). The age of the first suicide attempt was significantly higher among the suicide completers when compared to controls ($F=4.91$, $p=0.028$ when main effect tested individually; $F=8.02$, $p=0.005$ in full-factorial model).

Table 1: Personal History Results – The Overall Sample

| Characteristic | Yes/No Ratio (%) / Mean (s.d.) | | Results | |
|-----------------|-----------------------------------|-------------------|-----------------------------|-------------------------|
| | SC | CO | Statistic | Significance |
| Childhood abuse | 54/102 (35%) | 32/84 (28%) | $\chi^2= 1.52$ OR= 1.390 | 0.218 [0.823; |
| Previous SA | 42/131 (24%) | 5/104 (5%) | $_e$ OR= 6.669 | <0.001 [2.548;17.46] |
| Age at first SA | 39.44 (14.181) | 31.89 (11.728) | F= 4.910 | 0.028 |

The results of the single variable analysis pertaining to the personal history in the overall sample. Note regarding abbreviations: SA= suicide attempt(s); SC = suicide completers; CO = control participants; F = F-ratio test in an analysis of variance test (main effect tested individually); $_e$ =Fisher's exact test; χ^2 = Chi-Square ; OR=odds ratio. “Significance” refers to the p-value corresponding to each test, and, in the case of the odds ratio, to its 95% confidence interval limits. Yes/No Ratio refers to the raw numbers in that subsample for each categorical variable. For example, 54/102 in the SC childhood abuse category denotes the fact that the subsample of suicide completers for whom the information was recorded consisted in 54 individuals that had a history of childhood abuse and 102 that did not; in other words, 35% of the SC individuals for whom the information was recorded had a history of childhood abuse.

2.3.1.2 Psychopathology

With respect to axis I and axis II psychopathology, the results of the analyses on the overall sample are displayed in Table 2. The main effect of suicide group was significant ($p < 0.001$) with respect the number of lifetime axis I diagnoses (Mann-Whitney $z = -4.07$), of last 6 months axis I diagnoses (Mann-Whitney $z = -4.36$) and

axis II diagnoses. Depressed suicide completers displayed significantly higher odds than depressed controls for lifetime and last 6 months alcohol dependence, lifetime and last 6 months drug dependence, and for lifetime and last 6 months pathological gambling. Similarly, depressed suicide completers displayed significantly higher odds than depressed controls for any axis II disorder, any cluster A disorder, any cluster B disorder, as well as for antisocial personality disorder and for borderline personality disorder.

On the other hand, suicide completers did not display significantly higher odds than controls for meeting the criteria of lifetime or last 6 months anxiety disorder, any Cluster C diagnosis, eating disorder, or psychotic symptomatology.

Table 2: Psychopathology Results – The Overall Sample

| Diagnosis | Yes/No (%) or Rank | | Results | | |
|-----------------------------------|--------------------|--------------|-----------|-----------|----------------|
| | SC | CO | | Statistic | Significance |
| Axis I | | | | | |
| Alcohol dependence (lifetime) | 49/151 (25%) | 16/113 (12%) | $\chi^2=$ | 7.24 | 0.007 |
| Alcohol dependence (six-months) | 38/162 (19%) | 11/118 (9%) | OR= | 2.292 | [1.239;4.238] |
| Drug dependence (lifetime) | 30/171 (15%) | 9/120 (7%) | $\chi^2=$ | 6.79 | 0.009 |
| Drug dependence (six-months) | 22/179 (11%) | 4/125 (3%) | OR= | 2.516 | [1.235;5.127] |
| Anxiety (lifetime) | 40/160 (20%) | 21/108 (16%) | $\chi^2=$ | 0.719 | 0.397 |
| Anxiety (six-months) | 34/166 (17%) | 18/111 (14%) | OR= | 1.286 | [0.719;2.301] |
| Eating disorder | 3/198 (1%) | 1/128 (1%) | $\chi^2=$ | 0.547 | 0.460 |
| Psychotic symptoms | 22/179 (11%) | 15/114 (12%) | OR= | 1.263 | [0.680;2.347] |
| Gambling (lifetime) | 27/174 (13%) | 0/129 (0%) | $\chi^2=$ | 0.037 | 0.848 |
| Gambling (six-months) | 27/174 (13%) | 0/129 (0%) | OR= | 0.934 | [0.465;1.875] |
| No. axis I diagnoses (lifetime) | 0.89 (0.939) | 0.47 (0.708) | $\chi^2=$ | 1.741 | <0.001 |
| No. axis I diagnoses (six-months) | 0.71 (0.842) | 0.33 (0.575) | OR= | 1.741 | [1.580;1.919] |
| Axis II | | | | | |
| Antisocial personality disorder | 23/168 (12%) | 2/119 (2%) | $\chi^2=$ | 1.741 | <0.001 |
| Borderline personality disorder | 31/160 (16%) | 4/117 (3%) | OR= | 5.667 | [1.884;35.212] |
| Cluster A | 19/172 (10%) | 4/117 (3%) | $\chi^2=$ | 3.231 | <0.001 |
| Cluster B | 46/145 (24%) | 6/115 (5%) | OR= | 3.231 | [1.072;9.741] |
| Cluster C | 30/161 (16%) | 19/102 (16%) | $\chi^2=$ | 6.080 | <0.001 |
| Any axis II diagnosis | 82/109 (75%) | 22/99 (18%) | OR= | 6.080 | [2.509;14.736] |
| No. axis II diagnoses | 0.69 (0.998) | 0.31 (0.784) | $\chi^2=$ | 1.000 | 0.999 |
| | | | OR= | 20.419 | [0.535;1.871] |
| | | | $\chi^2=$ | 3.385 | 0.000006 |
| | | | OR= | 4.398 | [1.966;5.830] |
| | | | $\chi^2=$ | 2.130 | <0.001 |
| | | | OR= | 2.130 | <0.001 |

The results of the single variable analysis pertaining to axis I and axis II psychopathology. Note regarding abbreviations: SC = suicide completers; CO = control participants; no. = number (of); $_e$ =Fisher's exact test; χ^2 = Chi-Square ; z_{MW} = Mann-Whitney z score; z_{KS} = Kolmogorov-Smirnov z score; OR=odds ratio. Rank refers to mean ranking in non-parametric tests; Significance refers to the p-value corresponding to each test, and, in the case of the odds ratio, to its 95% confidence interval limits. Yes/No Ratio refers to the raw numbers in that subsample for each categorical variable.

2.3.1.3 Personality Traits and Behavioural Predispositions

The significant main effect of suicide status group was reflected in suicide completers scoring significantly higher on the BDHI hostility scales ($F=3.73$, $p=0.054$ and $F=5.67$, $p=0.018$ when the main effect was tested individually and in a full-factorial model, respectively). Also, suicide completers scored significantly lower on the self-directedness scale and marginally higher on perseverance. Depressed participants who had completed suicide displayed significantly higher odds than depressed controls for scoring high (above 75) on the BIS impulsivity scale.

Table 3: Personality and Behavioural Predispositions Results – The Overall Sample

| Characteristic | Yes/No Ratio, Mean Score (s.d.) or Ranking | | Results | | |
|--------------------------|--|--------------------|------------------------|-----------------|----------------------|
| | SC | CO | Statistic | Significance | |
| Impulsivity | 66.229 (13.656) | 65.354 (13.023) | F= | 0.270 | 0.604 |
| Impulsivity ≥ 75 | 47/101 (32%) | 23/87 (21%) | $\chi^2=$ OR= | 3.756 1.760 | 0.053 [0.99;3.13] |
| Hostility | 37.562 (14.101) | 34.165 (13.358) | F= | 3.733 | 0.054 |
| Aggressivity (lifetime) | 3.365 (4.112) | 2.621 (2.756) | $z_{MW}=$ $z_{KS}=$ | -0.656 0.853 | 0.512 0.461 |
| Aggressivity (adulthood) | 5.11 (5.020) | 4.01 (3.656) | $z_{MW}=$ $z_{KS}=$ | -1.403 0.815 | 0.160 0.521 |
| Harm avoidance | 19.034 (7.397) | 19.925 (7.038) | F= | 0.956 | 0.329 |
| Novelty seeking | 20.408 (7.498) | 20.019 (7.484) | F= | 0.226 | 0.635 |
| Self-directedness | 24.548 (8.017) | 26.8 (8.123) | F= | 4.847 | 0.029 |
| Reward dependence | 13.459 (4.452) | 14.25 (4.377) | F= | 1.958 | 0.163 |
| Cooperativeness | 28.698 (8.213) | 29.505 (6.679) | $z_{MW}=$ $z_{KS}=$ | -0.524 0.667 | 0.601 0.765 |
| Self-transcendence | 11.877 (6.799) | 11.95 (6.223) | $z_{MW}=$ $z_{KS}=$ | -0.248 0.715 | 0.805 0.687 |
| Perseverance | 5.287 (2.261) | 4.838 (2.200) | $z_{MW}=$ $z_{KS}=$ | -1.793 1.000 | 0.073 0.185 |

The results of the single variable analysis pertaining to personality and behavioural predispositions in the overall sample. Note: SC = suicide completers; CO = control participants; F = F-ratio test in an analysis of variance test (main effect tested individually); z_{KS} = Fisher's exact test; χ^2 = Chi-Square ; z_{MW} = Mann-Whitney z score; z_{KS} = Kolmogorov-Smirnov z score; OR=odds ratio. Significance refers to the p- value corresponding to each test, and, in the case of the odds ratio, to its 95% confidence interval limits. Yes/No Ratio refers to the raw numbers in that subsample for each categorical variable.

2.3.2 Effects after Stratification by Gender

2.3.2.1 Socio-demographic Characteristics and Personal History

A history of previous suicide attempts was more likely among depressed suicide completers than among their depressed counterparts, both in men and women ($p=0.001$ and $p = 0.002$, respectively). The age at first attempt tended to display an interaction between gender and suicide status ($F=3.08$, $p=0.081$, see Table 10) such that following stratification, the suicide/control difference was significant only among women ($F=7.99$, $p=0.008$) (see Table 4 and 5).

Table 4: Personal History Results – Subsample of Men

| Characteristic | Yes/No Ratio, | | Results | | |
|-----------------|------------------|------------------|-----------|--------------|------------------------|
| | SC | CO | Statistic | Significance | |
| Childhood abuse | 37/85 (30%) | 19/63 (23%) | $\chi^2=$ | 1.261 | 0.261 |
| Previous SA | 31/105 (23%) | 4/71 (5%) | OR= _e | 1.443 | [0.760;2.743] 0.001 |
| Age at first SA | 39.46 (14.58) | 35.00 (10.97) | F= | 1.322 | 0.252 |

The results of the single variable analysis pertaining to the personal history in the sample stratified by gender. Note regarding abbreviations: SA = suicide attempt(s); SC = suicide completers; CO = control participants; F = F-ratio test in an analysis of variance test (main effect tested individually); _e=Fisher's exact test; χ^2 = Chi-Square ; OR=odds ratio. Significance refers to the p-value corresponding to each test, and, in the case of the odds ratio, to its 95% confidence interval limits. Yes/No Ratio refers to the raw numbers in that subsample for each categorical variable.

Table 5: Personal History Results – Subsample of Women

| Characteristic or Diagnosis | Yes/No Ratio, Mean (s.d.) | | Results | | |
|-----------------------------|---------------------------|------------------|------------------|----------------|-------------------------|
| | SC | CO | Statistic | Significance | |
| Childhood abuse | 17/17 (50%) | 13/21 (38%) | $\chi^2=$ OR= | 0.954 1.615 | 0.329 [0.616;4.238] |
| Previous SA | 11/26 (30%) | 1/33 (3%) | $_e$ OR= | 13.962 | 0.002 [1.692;115.23] |
| Age at first SA | 39.31 (13.164) | 20.25 (5.909) | F= | 7.986 | 0.008 |

The results of the single variable analysis pertaining to the personal history in the sample stratified by gender. Note regarding abbreviations: SA = suicide attempt(s); SC = suicide completers; CO = control participants; F = F-ratio test in an analysis of variance test (main effect tested individually); $_e$ = Fisher's exact test; χ^2 = Chi-Square ; OR = odds ratio. Significance refers to the p-value corresponding to each test, and, in the case of the odds ratio, to its 95% confidence interval limits. Yes/No Ratio refers to the raw numbers in that subsample for each categorical variable.

2.3.2.2 Psychopathology

After stratification by gender, different patterns of comorbidity were observed in men and women (see Tables 6 and 7). Male suicide completers had higher odds ratios than male controls for last 6 months alcohol dependence, last 6 months drug substance dependence, but not for lifetime drug dependence ($p=0.143$), nor for lifetime alcohol dependence ($p=0.077$). On the other hand, female suicide completers had higher odds than controls for lifetime alcohol and drug substance dependence, but not for last 6 months diagnoses.

Table 6: Psychopathology Results – Subsample of Men

| Diagnosis | Yes/No, Rank | | Results | | |
|-----------------------------------|-----------------|----------------|------------------------|-----------------|--------------------------|
| | SC | CO | Statistic | Significance | |
| Axis I | | | | | |
| Alcohol dependence (lifetime) | 40/119 (25%) | 14/76 (16%) | $\chi^2=$ OR= | 3.120 1.825 | 0.077 [0.931;3.578] |
| Alcohol dependence (six-months) | 33/126 (21%) | 10/80 (11%) | $\chi^2=$ OR= | 3.741 2.095 | 0.053 [0.979;4.484] |
| Drug dependence (lifetime) | 23/137 (14%) | 8/82 (9%) | $\chi^2=$ OR= | 1.721 | 0.143 [0.736;4.025] |
| Drug dependence (six-months) | 17/143 (11%) | 3/87 (3%) | $\chi^2=$ OR= | 3.448 | 0.031 [0.982;12.105] |
| Anxiety (lifetime) | 28/131 (18%) | 11/79 (12%) | $\chi^2=$ OR= | 1.263 1.535 | 0.261 [0.724;3.254] |
| Anxiety (six-months) | 26/133 (16%) | 10/80 (11%) | $\chi^2=$ OR= | 1.276 1.564 | 0.259 [0.717;3.412] |
| Eating disorder | 1/159 (1%) | 0/90 (0%) | $\chi^2=$ OR= | 1.566 | 0.640 [1.426;1.719] |
| Psychotic symptoms | 17/143 (11%) | 10/80 (11%) | $\chi^2=$ OR= | 0.014 0.951 | 0.905 [0.416;2.176] |
| Gambling (lifetime) | 24/136 (15%) | 0/90 (0%) | $\chi^2=$ OR= | 1.662 | <0.001 [1.495;1.848] |
| Gambling (six-months) | 25/135 (16%) | 0/90 (0%) | $\chi^2=$ OR= | 1.667 | <0.001 [1.498;1.854] |
| No. axis I diagnoses (lifetime) | 182.01 | 141.58 | $z_{MW}=$ $z_{KS}=$ | -3.521 1.629 | <0.001 0.010 |
| No. axis I diagnoses (six-months) | 184.54 | 139.83 | $z_{MW}=$ $z_{KS}=$ | -4.040 1.961 | <0.001 0.001 |
| Axis II | | | | | |
| Antisocial personality disorder | 21/133 (14%) | 1/85 (1%) | $\chi^2=$ OR= | 13.421 | <0.001 |
| Borderline personality disorder | 25/129 (16%) | 1/85 (1%) | $\chi^2=$ OR= | 16.476 | <0.001 |
| Cluster A | 15/139 (10%) | 2/84 (2%) | $\chi^2=$ OR= | 4.532 | 0.024 [1.011;20.314] |
| Cluster B | 36/118 (23%) | 2/84 (2%) | $\chi^2=$ OR= | 12.814 | <0.001 [3.002;54.686] |
| Cluster C | 24/130 (16%) | 11/75 (13%) | $\chi^2=$ OR= | 0.346 1.259 | 0.557 [0.584;2.714] |
| Any axis II diagnosis | 65/89 (42%) | 13/73 (15%) | $\chi^2=$ OR= | 18.462 4.101 | 0.00002 [2.096;8.023] |
| No. axis II diagnoses | 169.88 | 127.62 | $z_{MW}=$ $z_{KS}=$ | -4.248 2.013 | <0.001 0.001 |

The results of the single variable analysis pertaining to axis I and axis II psychopathology in the sample stratified by gender. Note regarding abbreviations: no. = number (of); SC = suicide completers; CO = control participants; $_e$ = Fisher's exact test; χ^2 = Chi-Square; z_{MW} = Mann-Whitney z score; z_{KS} = Kolgomorov-Smirnov z score; OR = odds ratio; Rank refers to mean ranking in non-parametric test. Significance refers to the p-value corresponding to each test, and, in the case of the odds ratio, to its 95% confidence interval limits. Yes/No Ratio refers to the raw numbers in that subsample for each categorical variable.

Compared to depressed controls, male suicide completers also had higher odds ratios for lifetime and last 6 months pathological gambling, antisocial personality disorder, borderline personality disorder, any Cluster A disorder, any Cluster B disorder, and any axis II disorder, as well as a higher number of axis II diagnoses. Among women, none of these variables were statistically significant at a level of 95% confidence.

Table 7: Psychopathology Results – Subsample of Women

| Diagnosis | Yes/No or Rank | | Results | |
|-----------------------------------|----------------|----------------|--------------------------|-----------------------------------|
| | SC | CO | Statistic | Significance |
| Axis I | | | | |
| Alcohol dependence (lifetime) | 9/32 (22%) | 2/37 (5%) | \bar{e} OR= 5.203 | 0.029 [1.047;4.041] |
| Alcohol dependence (six-months) | 5/36 (12%) | 1/38 (3%) | \bar{e} OR= 5.278 | 0.112 [0.588;47.389] |
| Drug dependence (lifetime) | 7/34 (17%) | 1/38 (3%) | \bar{e} OR= 7.824 | 0.034 [0.915;66.880] |
| Drug dependence (six-months) | 5/36 (12%) | 1/38 (3%) | \bar{e} OR= 5.278 | 0.112 [0.588;47.389] |
| Anxiety (lifetime) | 12/29 (41%) | 10/29 (26%) | χ^2 = OR= 1.200 | 0.132 [0.448;3.212] |
| Anxiety (six-months) | 8/33 (20%) | 8/31 (21%) | \bar{e} OR= 0.939 | 0.566 [0.314;2.810] |
| Eating disorder | 2/39 (5%) | 1/38 (3%) | \bar{e} OR= 1.316 | 0.519 [0.574;3.018] |
| Psychotic symptoms | 5/36 (12%) | 5/34 (13%) | \bar{e} OR= 0.944 | 0.599 [0.251;3.554] |
| Gambling (lifetime) | 3/38 (7%) | 0/39 (0%) | \bar{e} OR= 2.026 | 0.130 [1.616;2.541] |
| Gambling (six-months) | 2/39 (5%) | 0/39 (0%) | \bar{e} OR= 2.000 | 0.259 [1.602;2.497] |
| No. axis I diagnoses (lifetime) | 177.83 | 140.00 | z_{MW} = z_{KS} = | -1.871 1.079 0.061 0.195 |
| No. axis I diagnoses (six-months) | 170.10 | 141.79 | z_{MW} = z_{KS} = | -1.439 0.593 0.136 0.874 |
| Axis II diagnoses | | | | |
| Antisocial personality disorder | 2/35 (5%) | 1/34 (3%) | \bar{e} OR= 1.943 | 0.521 [0.168;22.434] |
| Borderline personality disorder | 6/31 (16%) | 3/32 (9%) | \bar{e} OR= 2.065 | 0.268 [0.474;8.991] |
| Cluster A | 4/33 (11%) | 2/33 (6%) | \bar{e} OR= 2.000 | 0.364 [0.343;11.679] |
| Cluster B | 10/27 (27%) | 4/31 (11%) | \bar{e} OR= 2.870 | 0.084 [0.807;10.212] |
| Cluster C | 6/31 (16%) | 8/27 (23%) | \bar{e} OR= 0.653 | 0.340 [0.201;2.121] |
| Any axis II diagnosis | 17/20 (46%) | 9/26 (26%) | \bar{e} OR= 2.456 | 0.061 [0.907;6.650] |
| No. axis II diagnoses | 177.70 | 146.17 | z_{MW} = z_{KS} = | -1.654 0.858 0.098 0.453 |

The results of the single variable analysis pertaining to axis I and axis II psychopathology in the sample stratified by gender. Note regarding abbreviations: no. =number; SC = suicide completers; CO = control participants; _e=Fisher's exact test; χ^2 = Chi-Square ; z_{MW} = Mann-Whitney z score; z_{KS} = Kolgomorov-Smirnov z score; OR=odds ratio. Rank refers to mean ranking in non-parametric tests. Significance refers to the p- value corresponding to each test, and, in the case of the odds ratio, to its 95% confidence interval limits. Yes/No Ratio refers to the raw numbers in that subsample for each categorical variable.

2.3.2.3 Personality Traits and Behavioural Predispositions

Exclusively within the male subsample, suicide completers had significantly higher odds than controls if they had a high BIS score (see Table 8). None of the other personality and behavioural predisposition variables significantly differentiated between suicide completers and controls, among men.

However, the female suicide-versus-controls odds ratio was not significant for having a high BIS impulsivity score. Among women, suicide completers had significantly higher BDHI hostility scores ($F=4.84$, $p=0.032$), but not for any of the other variables (see Table 9).

Table 8: Personality and Behavioural Predispositions Results – Subsample of Men

| Characteristic | Yes/No Ratio, Mean Score (sd) or Mean Ranking | | Results | | |
|-----------------------------|---|-------------------|------------------------|-----------------|-----------------------|
| | SC | CO | Statistic | Significance | |
| Impulsivity | 67.24 (13.23) | 65.91 (12.77) | F= | 0.490 | 0.485 |
| Impulsivity score \geq 75 | 40/77 (34%) | 16/62 (21%) | $\chi^2=$ OR= | 4.275 2.013 | 0.039 [1.03; 3.93] |
| Hostility | 37.09 (14.08) | 35.31 (13.08) | F= | 0.774 | 0.380 |
| Aggressivity (lifetime) | 144.50 | 141.62 | $z_{MW}=$ $z_{KS}=$ | 0.206 0.614 | 0.836 0.845 |
| Aggressivity (adulthood) | 146.31 | 134.41 | $z_{MW}=$ $z_{KS}=$ | -1.070 0.673 | 0.285 0.755 |
| Harm avoidance | 18.607 (7.704) | 19.807 (7.091) | F= | 1.216 | 0.272 |
| Novelty seeking | 20.805 (7.734) | 19.155 (7.368) | F= | 2.241 | 0.136 |
| Self-directedness | 24.623 (8.075) | 26.148 (7.359) | F= | 1.774 | 0.185 |
| Reward dependence | 12.9 (4.464) | 13.288 (4.502) | F= | 0.350 | 0.555 |
| Cooperativeness | 119.12 | 117.98 | $z_{MW}=$ $z_{KS}=$ | -0.114 0.899 | 0.909 0.395 |
| Self-transcendence | 115.56 | 119.63 | $z_{MW}=$ $z_{KS}=$ | -0.441 0.848 | 0.659 0.468 |
| Perseverance | 134.83 | 122.74 | $z_{MW}=$ $z_{KS}=$ | -1.165 0.896 | 0.244 0.398 |

The results of the single variable analysis pertaining to personality and behavioural predispositions in the sample stratified by gender. Note Note regarding abbreviations: SC = suicide completers; CO = control participants; F = F-ratio test in an analysis of variance test (main effect tested individually); χ^2 = Chi-Square ; z_{MW} = Mann-Whitney z score; z_{KS} = Kolgomorov-Smirnov z score; OR=odds ratio. Significance refers to the p- value corresponding to each test, and, in the case of the odds ratio, to its 95% confidence interval limits. Yes/No Ratio refers to the raw numbers in that subsample for each categorical variable.

Table 9: Personality and Behavioural Predispositions Results – Subsample of Women

| Characteristic | Yes/No Ratio, Mean Score (sd) or Mean Ranking | | Results | | |
|-----------------------------|---|--------------------|---------------------|--------------|-------------------------|
| | SC | CO | Statistic | Significance | |
| Impulsivity | 62.389 (14.424) | 64.009 (13.734) | F= | 0.209 | 0.650 |
| Impulsivity score \geq 75 | 7/24 (23%) | 7/25 (22%) | _e OR= | 1.042 | 0.592 [0.318; 3.417] |
| Hostility | 39.39 (14.28) | 31.45 (13.80) | F= | 4.841 | 0.032 |
| Aggressivity (lifetime) | 137.74 | 124.86 | z_{MW} = | -0.670 | 0.503 |
| | | | z_{KS} = | 0.779 | 0.579 |
| Aggressivity (adulthood) | 141.01 | 124.95 | z_{MW} = | -0.905 | 0.366 |
| | | | z_{KS} = | 0.459 | 0.984 |
| Harm avoidance | 20.536 (6.070) | 20.202 (7.005) | F= | 0.042 | 0.838 |
| Novelty seeking | 19.041 (6.551) | 22.068 (7.461) | F= | 3.089 | 0.084 |
| Self-directedness | 24.276 (7.935) | 28.373 (9.665) | F= | 3.306 | 0.074 |
| Reward dependence | 15.425 (3.868) | 16.475 (3.133) | F= | 1.482 | 0.228 |
| Cooperativeness | 141.03 | 153.93 | z_{MW} = | -0.587 | 0.557 |
| | | | z_{KS} = | 0.634 | 0.817 |
| Self-transcendence | 127.63 | 121.38 | z_{MW} = | -0.234 | 0.815 |
| | | | z_{KS} = | 0.635 | 0.814 |
| Perseverance | 149.50 | 118.00 | z_{MW} = | -1.518 | 0.129 |
| | | | z_{KS} = | 1.244 | 0.091 |

The results of the single variable analysis pertaining to personality and behavioural predispositions in the sample stratified by gender. Note regarding abbreviations: SC=suicide completers; CO = control participants; F = F-ratio test in an analysis of variance test (main effect tested individually); _e=Fisher's exact test; χ^2 = Chi-Square ; z_{MW} = Mann-Whitney z score; z_{KS} = Kolgomorov-Smirnov z score; OR=odds ratio. Significance refers to the p- value corresponding to each test, and, in the case of the odds ratio, to its 95% confidence interval limits (sd=standard

deviation). *Yes/No Ratio* refers to the raw numbers in that subsample for each categorical variable.

The two-way analysis of variance revealed a significant interaction effect (see Table 10) between gender and suicide status group on novelty seeking scores ($F=8.25, p<0.001$), within the full factorial models. In the models containing only the interaction effect, significance was observed for reward dependence ($p<0.001$), but this effects was no longer significant in the full factorial model (i.e. after controlling for the main effects of the suicide status group and of gender).

Table 10: Interaction effects resulting from the two-way analysis of variance.

| Characteristic | Full Factorial Models | | Individual Tests | |
|-------------------|---|--------------|---|--------------|
| | Gender - Suicide Status Interaction Effects | | Gender - Suicide Status Interaction Effects | |
| | Statistic | Significance | Statistic | Significance |
| Age at first SA | F= 3.078 | 0.081 | F= 2.970 | 0.034 |
| Impulsivity | F= 0.580 | 0.447 | F= 1.000 | 0.267 |
| Hostility | F= 2.278 | 0.132 | F= 2.000 | 0.104 |
| Harm avoidance | F= 0.548 | 0.460 | F= 0.925 | 0.429 |
| Novelty seeking | F= 4.347 | 0.038 | F= 1.665 | 0.175 |
| Self-directedness | F= 1.186 | 0.277 | F= 2.238 | 0.084 |
| Reward dependence | F= 0.286 | 0.593 | F= 8.249 | <0.001 |

For all of the continuous variables that did not markedly deviate from normality, we calculated the interaction effect between suicide status group (i.e. suicide completer versus control) and gender (male versus female) on the score of the respective

variable. The right half of the table displays the results for the test performed individually (the interaction as a single parameter and the continuous variable as a dependent variable). The left half of the table displays the interaction results when the interaction was tested within a full factorial model (i.e. along with the effect of group and the effect of gender as parameters). Note regarding abbreviations: SA denotes suicide attempt(s).

2.3.5 Multiple Variable Analysis

In the first block of the multiple logistic regression, we included the gender interactions with the following candidate variables: having previously attempted suicide, lifetime alcohol dependence, lifetime drug substance dependence, last 6 months alcohol dependence, last 6 months drug substance dependence, anxiety disorders, Cluster A diagnosis, and Cluster B diagnosis, and gambling (N=275). This procedure resulted in a model that included the gender interactions with having previously attempted suicide, Cluster B diagnosis, and gambling. However, only the former two effects were significant. Thus, they were selected for the next step. In the next block, we added to these variables the main effects of the same nine variables. The resulting effects were as follows: the gender - previous suicide attempt interaction, the gender - Cluster B diagnosis interaction, previous suicide attempt, Cluster A, and lifetime gambling. After selecting only the variables significant at $p < 0.10$, the following parameters remained in the final model: Cluster B diagnosis – gender interaction, Cluster A and previous suicide attempt. In other words, both men and women had an odds for being among the suicide completers

approximately nine times higher if they met the criteria for a Cluster A diagnosis, and about five times higher if they had previously attempted suicide.

After controlling for the effects of Cluster A diagnosis and previous suicide attempts, gender still added significant moderation to the effect of having met the criteria for Cluster B diagnosis. Thus, the odds ratio for being a suicide completer rather than a control participant, if meeting Cluster B diagnosis criteria, is about 19 times higher in men than in women.

2.4 Discussion

In our case-control study of depressed participants, the overall sample which included both men and women revealed that, when compared to community controls, suicide completers had a significantly higher number of lifetime and last 6 months axis I diagnoses, higher number of axis II diagnoses, higher score of BDHI hostility, as well as higher odds to meet criteria for lifetime and last 6 months alcohol dependence, lifetime and last 6 months drug substance dependence, lifetime and last six-months gambling, antisocial personality disorder, borderline personality disorder, Cluster A diagnosis, Cluster B diagnosis, any SCID II diagnosis, and a high BIS impulsivity score. However, suicide completers had lower scores on self-directedness. These results are concordant with previous studies on depressed suicidal behaviours and show that psychopathology related to impulse dyscontrol may be a crucial factor in determining suicidal completion.

No significance was found in our overall sample of depressed participants, or for both genders separately, for history of childhood abuse, anxiety, psychotic symptoms, or for any cluster C diagnosis. These results add to the current divide in the evidence concerning the contribution of anxiety to suicide completion, and suggest that even after controlling for the effect of MDD, both anxiety and childhood abuse are no longer significant in increasing the odds for suicide in either gender.

However, in the overall sample as well as among men and women separately, the suicide-to-control odds ratio was significant for having attempted suicide previously. This replicates previous findings showing that history of previous suicide attempts is predictive of suicide completion at follow-ups up to six years (Suominen, et al., 2004), and differentiates between cases and controls among men (Grøholt, Ekeberg, Wichstrøm, & Haldorsen, 1999) and women (Grøholt, et al., 1999) in adolescent samples. Our result may however be related strongly to the fact that, in our sample, only a few participants in the control group (four among men and one among women) showed a history of previously having attempted suicide. This, in turn, may merely be a result of the recruitment process, which relied on outpatient services. It would be of interest to delineate, in the future, the impact of interactions between gender, nonfatal suicidal behaviour and depression on fatal acts. Although some studies have shown that women suicide completers more frequently present with a history of suicide attempts than men suicide completers (Brent, et al., 1999;

Salib & Green, 2003), it is unclear to what extent these results are mediated by psychopathology. Future studies on this topic may benefit from choosing a sample that is representative with regards to suicide attempt and self-harm behaviours, both among men and women, such that cross-gendered comparisons could shed light on causal factors being mediated or moderated by depression.

After stratification by gender, some different patterns of morbidity were observed in men and women. Only among men did suicide completers have significantly higher odds compared to controls for meeting the criteria for last 6 months gambling, antisocial personality disorder, borderline personality disorder, Cluster A diagnosis, Cluster B diagnosis, and high impulsivity scores. Among women, the odds ratios were only marginal for any axis II diagnosis ($p=0.06$) and Cluster B diagnosis ($p=0.08$). Female suicide-versus-controls odds ratio was neither significant for meeting the criteria for antisocial personality disorder, borderline personality disorder, nor for lifetime and last 6 months gambling. In line with studies showing increased rates of hostility, aggression and cluster B diagnoses among men in community samples, these results support the notion that impulse dyscontrol may be related to suicide, particularly for men.

The multiple variable (logistic regression) analysis revealed that after controlling for the effects of Cluster A diagnosis and previous suicide attempts, gender significantly moderates the effect of Cluster B diagnosis. Thus, while both men and women may be at a higher risk for suicide if meeting the criteria for a

Cluster B diagnosis, the increase in risk is markedly higher in men than in women. In fact, exploratory analyses controlling for the main effect of cluster B disorders clearly show that the interaction with gender does remain significant. Consequently, meeting the criteria for a Cluster B diagnosis is a suicide risk factor with significant specificity to men, and gender moderates the impact of comorbidity with a Cluster B diagnosis in predicting suicide completion among depressed individuals over and beyond the main effect of previously having attempted suicide. Evidently, these results speak to the gender paradox in suicide. While many risk factors for attempting suicide may be specific to women, the implication is that in men, this risk may be overcome by their higher likelihood to deviate with respect to Cluster B diagnoses, and as a consequence, men complete suicide more frequently.

With respect to meeting criteria for alcohol dependence and/or drug substance dependence in the last six months, the odds were significantly higher for suicide completers versus controls only among men. Conversely, in the single variable analysis, lifetime alcohol and drug substance dependence increased the odds for being among the suicide completers, rather than controls, only among women (men displaying a marginal effect for lifetime alcohol dependence ($p=0.08$)). It is thus the substance-related, more chronic conditions that may be specific to women's risk for suicide. The fact that the effect was reversed for current alcohol and drug substance dependence seems to support the hypothesis that

impulse-related conditions, rather than chronic consequences of impulsive behaviours, constitute the risk for suicide in men.

As shown by the results of the two-way analysis of variance, the personality traits and behavioural predispositions paint a more complex picture. Neither the main effect of suicide status group, the simple effect stratified by gender, nor the interaction effect between gender and suicide group were significant for impulsivity scores. On the other hand, impulsivity did significantly differentiate between suicide completers and control participants in the overall sample and the male subsample, when considering the high (≥ 75) scores on the BIS scale. These results suggest that gender may moderate the relationship between suicide status group and impulsivity, and moreover, mirror and support the results related to cluster B personality diagnoses.

Both in the overall sample and among women separately, hostility (BDHI) scores differentiated between suicide completers and control participants ($p=0.054$, $p=0.032$). However, the interaction effect between suicide status group and gender was not significant when tested individually ($p=0.104$), nor when tested along with the gender and suicide group effects ($p=0.132$). Therefore, although hostility scores may contribute to suicide completion in general, and more specifically for women, it is unlikely that gender moderates the relationship between suicide completion and BDHI hostility independently from MDD.

Suicide completers did not show overall significant differences in their novelty seeking scores compared to controls. While this result was replicated in the male subsample, the difference was only marginally significant ($p=0.084$) among women. In addition, as tested in the full factorial two-way ANOVA, the interaction effect between gender and suicide group remained significant ($F=4.35$, $p=0.038$) further suggesting that diminished novelty seeking may influence the pathway to suicide in women, but not for men.

Suicide completers were significantly less self-directed in comparison with control participants (see Table 3). The female suicide completers were only marginally different from controls and the interaction between gender and suicide group tended to be significant ($F=2.24$, $p=0.084$) when tested individually. However, after testing the interaction effect in a full factorial model, in which we included the effect of suicide group and gender, this tendency dissipated ($F=1.19$, $p=0.277$). Therefore, the effect of gender on the relationship between self-directedness and suicide completion may be masked by the general predisposition of those completing suicide to be less self-directed than their depressed counterparts.

When testing the gender–suicide status interaction effect individually, significance was found with respect to reward dependence ($F=8.25$, $p<0.001$). Previous studies in our research group have highlighted a gender difference with respect to self-directedness among suicide completers (McGirr, et al., 2006). Indeed, the gender main effect was also significant in this study of depressed individuals

($F=23.42$, $p<0.001$). However, once the main effects of gender and the suicide status group were included in the full factorial model, the interaction effect was no longer significant ($F=0.29$, $p=0.593$). This was further evidenced by the similarly non-significant results in men and women separately, suggesting that gender may not moderate the relation between reward dependence and suicide completion.

The major advantage of our study is that an important confounding variable in suicide completion research – the presence of major depression disorder – was controlled for by design. Moreover, the methodological robustness of our study is rooted in the standardized assessment of all variables, clearly due to the application of the psychological autopsy protocol for both axis I and axis II diagnoses, as well as with the behavioural and personality scales to all participants. The psychometric appeal of this study lies in the assessment of many conditions tapping different behavioural, temperamental, character and syndromatic aspects of the same trait – namely impulsive-aggressiveness. On the other hand, the theoretical strength and contribution of the study is in its exploration and demonstration of the moderating effect of gender on the mediating role of cluster B psychopathology in suicide completion.

Future research may be inspired by the explanatory pathways left uncertain in our study due to certain limitations. For instance, we did not take axis III diagnoses into consideration. Indeed, medical illness may be a factor confounding the effect of aggressive-impulsive morbidity on fatal suicide, and by consequence its

gender specificity. This type of stress may be indicative of perseverance-related and impulsiveness-related suicidal behaviour, as well as of risks that are specific to women. Studies investigating gender differences in the onset of depression have suggested that women are more sensitive to stress (Nazroo, et al., 1997; Piccinelli & Wilkinson, 2000) despite the fact that women do not have higher rates of adverse life events. Although, women do seem to react more intensely and seem to show a closer association between the life event and the onset of depression (Piccinelli & Wilkinson, 2000). Moreover, with respect to suffering from depression, women seem to be more sensitive to the effect of adverse childhood events including sexual abuse (Veijola, et al., 1998).

An interesting finding of this study is that chronic stress in the form of a history of childhood abuse did not increase the odds of suicide completion group membership in either men or women. Recent acute stress could however be an important factor in the gender paradox of suicide, and as suggested, may underscore the influence of impulsive-aggressive behaviours in suicidal mediation.

Although MDD diagnosis was controlled for in the study, we did not include a measure of depression severity – it is conceivable that suicide completers may be more severely depressed compared to control participants, which may in turn confound the gender moderation effect on cluster B comorbidity in increasing risk for suicide completion. Moreover, medication status, which was not a predictor in the study, may be more present among women and control participants, a situation

that would heighten the difference in Cluster B comorbidity among the four groups. All the same, forthcoming studies should incorporate severity, duration, and type of depressive symptomatology; as well as medication and acute and chronic stress in their explanatory models.

Most importantly, future studies may wish to build on the current methodological strength of our study and explore prospective analyses which would help clarify the complex relationship between gender, depression and its psychological comorbidities in their contribution to suicide completion. As a result, specific and sensitive prevention of this unnecessary fatality would be considerably improved.

Chapter 3 SUMMARY AND DISCUSSION

The current project consisted in a case-control psychological autopsy study of depressed men and women who committed suicide and their living depressed counterparts. Capitalising on the premise that considerations of gender differences in psychopathology are essential for understanding gender differences in suicide completion, the rationale of the case-control study aimed to improve both in method and in thematic scope the problems that were identified in the background literature. Previously it had been shown that the majority of suicide completers commonly present with major depressive disorder, and that while women suicides are more likely to suffer from major depression disorder, men suicides are more likely to meet criteria for substance, personality and childhood disorders (Arsenault-Lapierre, et al., 2004; Kim, et al., 2003; Shaffer, et al., 1996).

According to the findings of previous cross-sectional studies focusing on gender and suicide completion, men seemed to display higher scores of impulsivity (McGirr, et al., 2006), lifetime alcohol misuse and substance misuse disorders (McGirr, et al., 2006; Rich, et al., 1988) compared to women, with alcoholism sometimes interacting with age among certain clinical populations (Heilä, et al., 1997). Alcohol or substance use disorders interacts with gender (Suominen, et al., 2004), and accounts for the suicide-gender interaction (Young, et al., 1994) in cohort studies of gender and suicide. Moreover, case control studies of gender and suicide suggest that risk for suicide completion given by personality psychopathology is gender-specific, where conduct and disruptive disorders are more strongly

associated with SC among men than women (Brent, et al., 1999; Grøholt, et al., 1999). Given the reliance on youth samples in these latter studies, replication in adults was sought out by the present case-control study, in which all participants were above 17 years of age.

While many risk factors were significantly associated with suicide completion in both genders, many differences between genders have remained inconclusive given the multitude of conflicting findings resulting from different samples and different methodological approaches in previous studies (Agerbo, 2005; Ang, Chia, & Fung, 2006; Brent, et al., 1999; Grøholt, et al., 1999; Heilä, et al., 1997; Kung, Pearson, & Liu, 2003; Kwan, Ip, & Kwan, 2005; Marttunen, et al., 1995; McGirr, et al., 2006; O'Connor & Sheehy, 1997; Preti & Miotto, 1998; Qin, et al., 2000; Quan & Arboleda-Florez, 1999; Rich, et al., 1988; Salib & Green, 2003; Skogman, et al., 2004; Suominen, et al., 2004; Värnik, et al., 2008; Young, et al., 1994). To establish the specificity of different risk factors with respect to suicide completion in men and women, standardized psychopathologic assessments are necessary. Parsing out individual effects might then be pursued by controlling for the effects of causal factors that are differentially distributed across genders. However, none of the previous case-control studies investigating gender and suicide completion methodologically controlled for the presence of axis-I psychopathology (Agerbo, 2005; Brent, et al., 1999; Grøholt, et al., 1999; Kung, et al., 2003; Kwan, et al., 2005; Qin, et al., 2000), and moreover, only two included post-mortem DSM assessments

of psychopathology (Brent, et al., 1999; Grøholt, et al., 1999). As a methodological improvement, the present case control study set out to use standardized psychological autopsy assessments to parse out the different roles of various Axis I and II psychopathologies and personality predispositions in the two genders while controlling for major depressive disorder.

The results of the study support the view that impulse dyscontrol may be related to suicide, particularly in men. After stratification by gender, some different patterns of morbidity were observed in men and women. Only among men did suicide completers have significantly higher odds compared to controls for meeting the criteria for last six-months gambling, antisocial personality disorder, borderline personality disorder, Cluster A diagnosis, Cluster B diagnosis, and high impulsivity scores. Among women, the odds ratios were only marginal for any axis II diagnosis ($p=0.06$) and Cluster B diagnosis ($p=0.08$). Moreover, among both women and men separately, the suicide-to-control odds ratio was significant for having attempted suicide previously.

The major finding among men was that depressed suicides differed from depressed controls in their likelihood of meeting the criteria for a Cluster B personality disorder, and for high impulsivity scores. The Cluster B effect may have particular prominence in men, given the characteristics of the control group. Indeed, depressed men may in general be predisposed to personality disorders to a lesser extent than women, explaining the difference between genders with respect to

borderline personality disorder. In turn, although depressed men are more prone to antisocial personality disorder than women, they may also be less likely to seek help, compared to women, thereby increasing the suicide-versus-depressed controls discrepancy among men, rather than women.

On the other hand, the major finding among women was in their higher likelihood of lifetime substance dependence and higher hostility scores. This result may be analogous to the previous finding that violent women are more likely to differ from the norm of their gender in terms of antisocial personality disorder, than are violent men (Bland & Orn, 1986). Similarly, given that women are less likely to experience lifetime alcohol and substance dependence than men in the general population, as well as among depressed individuals, they are also more likely to differ from this norm when it comes to acts of fatal violence against the self: suicide. It is perhaps for this reason that not only large but also small increments of change along the BDHI hostility continuum are noticeable among women.

It is notable that Cluster B diagnosis was significant among men and marginal among women, bringing about the argument that impulse dyscontrol is important for both men and women, though it may be so to a different extent. Indeed, the multivariate analysis showed that Cluster B diagnoses may play a particularly severe role in men, after controlling for the effects of Cluster A diagnosis and previous suicide attempts. Similarly, aggressive-impulsive predispositions and behaviours may affect both men and women, albeit the former

may be more likely to predict suicide completers among depressed individuals if they have high impulsivity scores and recent substance dependence, and the former in general BDHI hostility scores and lifetime diagnosis of substance dependence.

To address the gender paradox, the multiple variable (logistic regression) analysis revealed that after controlling for the effects of Cluster A diagnosis and previous suicide attempts, gender significantly moderates the effect of Cluster B diagnosis. Thus, while both men and women may be at higher risk for suicide if meeting the criteria for a Cluster B diagnosis, the increase in risk is much higher in men than in women. In fact, in exploratory analyses controlling for the main effect of cluster B disorders, the interaction with gender remained significant. Thus, meeting the criteria for a Cluster B diagnosis is a suicide risk factor with significance specificity for men, and gender moderates the impact of comorbidity with a Cluster B diagnosis in predicting suicide completion among depressed individuals over and beyond the main effect of previously having attempted suicide.

With respect to meeting criteria for alcohol dependence and/or substance dependence in the last six months, the odds were significantly higher for suicide completers versus controls only among men. Conversely, in the single variable analysis, lifetime alcohol and non-alcohol substance dependence increased the odds for being among the suicide completers rather than controls only among women (men displaying a marginal effect for lifetime alcohol dependence ($p=0.08$)). It is

thus the more chronic substance-related conditions that may be specific to women's risk for suicide.

The present study also suggests that some personality traits that may overlap with the phenomenology of depression may also be involved in profiling suicide completers. For example, women suicide completers also had marginally lower novelty seeking scores, the suicide-gender interaction effect being significant after controlling for the main effects of gender and of suicide group (in the two-way analysis of variance predicting novelty seeking scores). In fact, the novelty seeking – gender interaction was also significant after controlling for the main effect of novelty seeking (in a logistic regression predicting suicide group). This suggests that novelty seeking may be an alarm signal of suicide risk particularly among depressed women. It can be argued that while impulsive-aggressive characteristics of depressed individuals are specific to men, traits related anhedonic, apathetic and hopelessness aspects of depression might be specific to women. Future studies may explore this relationship.

Similarly, the present results also suggest that gender may moderate the effect of characteristics related to self-directedness in comorbidity with depression in women. Although the full-factorial analysis did not reveal significance in the suicide-gender interaction, but only in the main effect, the gender – suicide interaction was significant in the individual analysis of variance model, the gender – self directedness interaction was significant after control for the main effect of self-

directedness, and self-directedness had a marginal effect among women. In line with previous investigations suggesting that the self-directedness may be particularly associated with depression given its cognitive nature and its potential impact on depressogenic attitudes (Richter & Eisemann, 2002), the present study may suggest that these, in turn may play a particular role in women, who are more prone to experiencing depression in the general population.

The personality traits and behavioural predispositions painted a complex picture in the results of the two-way analysis of variance. While the interaction with gender was not significant for impulsivity and hostility scores, high impulsivity scores (≥ 75) were associated with SC only in men, and hostility scores significantly differentiated between SC and controls only in women. However, the latter result contradicts the lack of significance in the interaction effect, suggesting that it may not be a robust gender difference, but rather a general difference between suicides and controls among depressed subjects.

The major advantage of our study is that an important confounding variable in suicide completion research – the presence of major depressive disorder – was controlled for by design. Future explorations may also consider measures of depression severity, axis III diagnoses, medication status and stressful precipitators.

Our results in relation to childhood abuse may be seen as running counter to expectations formed based on previous studies. These have confirmed that childhood maltreatment, including emotional, physical and sexual abuse, is a

substantial correlate of youth and adult suicide ideation and attempts (J. Brown, Cohen, Johnson, & Smailes, 1999) (Kaplan, Pelcovitz, & Labruna, 1999) (Santa Mina & Gallop, 1998). Gender differences in non-fatal suicidal behaviour among adolescents have also been observed to be different among the two genders with respect to the effects of sexual abuse, such that this characteristic was significantly associated with self injury in men and with self injury, suicide ideation and suicide attempt in women (Matsumoto, et al., 2009). Moreover, childhood sexual abuse significantly increased the odds for later suicide attempts, even after controlling for lifetime psychiatric illnesses (Davidson, et al., 1996; Molnar, Berkman, et al., 2001), and especially among women (Davidson, et al., 1996). This is of particular importance for our results, since we controlled for MDD.

However, the investigations into the relationship between suicide and childhood abuse have focused on non-fatal suicidal behaviour, rather than suicide completion. An indication of this fact is that, in a systematic review of studies on suicidality and childhood abuse, no studies published between 1988 and 1998 were identified (Santa Mina & Gallop, 1998). Since then, a psychological autopsy investigation was performed on childhood abuse and suicide completion, finding a significant association between childhood abuse and suicide completion, such that a history of childhood abuse was more frequent among suicide completers than among psychiatric controls, and, in turn more so than among community controls (Ostovar, 2009). Although this association was, thus, demonstrated to be present

independently from Axis I and Axis II psychopathology, the study did not specifically control for major depression disorder (Ostovar, 2009), which, in turn, is the novelty in our study. The current results add to previous information by demonstrating that, after controlling for major depression disorder, childhood abuse does not differentiate between SC and CO, as assessed via the psychological autopsy method.

It is noteworthy that an independent link between childhood abuse and suicidal completion has not unanimously been established, however. Some investigations did not find a clear link between childhood sexual abuse and suicide attempts or ideation ((Peters, 1988; Sedney & Brooks, 1984; Stepakoff, 1998)as discussed in (Santa Mina & Gallop, 1998)). In Kaplan et al's (1997) study, history of physical abuse displayed no association with a higher rate of suicide attempts, but rather with risk factors for suicide, such as depression and substance dependence (Kaplan, Pelcovitz, Salzinger, Mandel, & et al., 1997). Indeed, depression has been documented to be related to childhood abuse. Patients with a history of emotional abuse, neglect and/or physical abuse show higher rates, severity and incidence of depression episodes (Bernet & Stein, 1999; Fergusson, Boden, & Horwood, 2008; Gladstone, Parker, Wilhelm, Mitchell, & Austin, 1999), and depressed patients with a history of childhood sexual abuse are at higher risk for comorbidity (Zlotnick, Mattia, & Zimmerman, 2001). Thus, there is a case of the strong mediating role of depression in the effect of childhood abuse on later suicide completion. Note that

the fact that a history of suicide attempts was scarce in the control group may further suggest the specificity of depression as a mediator along the childhood abuse – suicide completion pathway.

Previous studies suggest that women are more sensitive to stress in relation to the onset of depression (Nazroo, et al., 1997; Piccinelli & Wilkinson, 2000) and to the effect of adverse childhood events, including sexual abuse, on subsequent depression (Veijola, et al., 1998), and thus that history of sexual or physical trauma is a risk factor for attempted suicide in depressed women (Brent, et al., 2002). An interesting finding of this study is that chronic stress in the form of a history of childhood abuse did not increase the odds of suicide completion group membership in either men or women. Recent acute stress could however be an important factor in the gender paradox of suicide, and as suggested, may underscore the influence of impulsive-aggressive behaviours in suicidal mediation.

Moreover, though it has previously been suggested that the impact of childhood abuse may be more severe among women, with respect to suicidal behaviour (Modestin, Oberson, & Erni, 1997; Windle, Windle, Scheidt, & Miller, 1995), we found no significance for suicide completion, in neither the male, nor the female subsample. This may indicate that the relation of childhood abuse to later suicide completion may be different from that to later suicide attempt, at least in regards to gender differences. On the other hand, some have found a relation between sexual abuse and suicidality only among men (Read, 1998). Comparisons

with community samples and investigations of different suicidal behaviours may shed more light into this matter, as well.

Our results did not reveal significant associations of suicide with childhood abuse in neither men nor women, thus did not replicate the results of Brent et. al. (1999) who found associations for lifetime abuse for both men and women in the psychological autopsy of adolescents (and for current abuse only in men). It remains to be investigated as to what degree depression and age interact to influence the relation between suicide and childhood abuse in men and women.

Keeping in mind that childhood abuse has been operationalised in many different ways in studies of suicidal behaviour (Santa Mina & Gallop, 1998), the extent to which our results may be compared to previous studies is limited by the nature of our 1-item assessment. First, the nature of the abuse (physical, psychological, or emotional; single event or chronic) was nonspecific in our study. Of particular interest is that, in a previous study, suicide completers scoring higher than the 70th percentile on the BIS were more likely to have had a history of severe indifference, rejection or negligence from either parent, but not of lack of parental affection, parental psychological violence, sexual abuse, or severe physical abuse (Zouk, Tousignant, Seguin, Lesage, & Turecki, 2006). Similarly, among suicide completers assessed with the Childhood Experiences of Care and Abuse (CECA) interview (Bifulco, Brown, & Harris, 1994), six-months anxiety disorder and a Cluster B disorder differentiated only between those with and those without any

childhood abuse; no significant relationship was found between psychiatric disorders and different subtypes of abuse – physical, sexual, family discord or parental neglect (Ostovar, 2009). In our study, no significant differences were found between suicide completers and controls in the 1-item assessment of childhood abuse, despite significant results with respect to high BIS scores. This may suggest that the general nature of the question may have masked any specificity of suicide completion with regard to different aspects of abuse. It is, then, difficult to ascertain to what extent childhood abuse of different types and severities affects the intricate relation between gender, depression and suicide completion.

Of notable interest, delinquency has also been shown to be associated with suicide attempts and sexual abuse in men, and, in addition, to self-injury and suicide ideation in women adolescents (Matsumoto, et al., 2009), suggesting a possible link between hostility, gender and suicidal behaviour. Future studies, including community control participants, may elucidate to what extent childhood abuse (of different severities and types) and gender interact to differentiate between later depression, suicide attempts and suicide completion.

Second, the identity of the abuser was not recorded in our study. Indeed, it has been confirmed that the identity of the abuser is a moderator of the relationship between abuse frequency and suicide attempts, the highest risk being conveyed by abusers from within the immediate family (Brezo, et al., 2008). Third, given the proxy-based nature of our assessment, we were unable to dissociate with our item

whether the value recorded referred to an objective meaning of childhood abuse (whether abusive events occurred), or a subject one (whether the person was perceived as an abused individual). Previous inquiry into this differentiation has shown that the rates of sexual abuse differ according to which definition is used (Carlin & Ward, 1992 as described in Santa Mina, 1998).

Several scholars have pointed towards the importance of considering environmental, as well as individual factors, when thinking about childhood trauma and suicidal behaviour (Adams & Lehnert, 1997) (the person-environment interactional paradigm). Indeed, future studies may inquire into the possibility that childhood abuse history among SC may be related to environmental factors that are common to those experienced by the depressed control participants; the difference between the groups may lie in different protective and coping mechanisms, or other risk factors unrelated to childhood abuse environments. This may explain why, after controlling for MDD, no differences were found to significantly differentiate the cases from the controls. Concordantly, despite the fact that family history of suicide may predict suicide completion independently of severe mental disorder (Runeson & Asberg, 2003), the familial transmission of suicide attempts, of mood disorders and of sexual abuse may be highly related (Brent, et al., 2002).

Finally, the psychological autopsy method may bias a 1-item assessment of childhood abuse such as ours. It is conceivable to argue that the rate of childhood abuse reported by proxies, months after the suicide, is minimized by the fact that the

report cannot be corroborated by the victim and the guilt experienced by the proxy is greater than for an alive participant. On the other hand, following this train of thought, the childhood abuse reports for MDD index participants may be more accurately reported by proxies, as the answer could be corroborated by victim and the guilt experience by the proxy is lower relative to the one for the SC group. To this extent, longitudinal studies of suicide completion and childhood abuse would not only delineate moderating and mediating factors, but would also provide an alternative to the methodological limitations inherent in the retrospective methods.

There are some disadvantages in understanding abnormal personality within the categorical model of personality disorders such as that reflected by the DSM-IV-TR (APA, 2000) Axis II psychopathologies. More than 60% of patients with personality disorders may also meet the criteria for one or more comorbid personality disorder categories (Flick et al., 1993). Moreover, there is low agreement in detecting the presence of any personality disorder (with kappa values between 0.08 and 0.54) (Perry, 1992).

It has been argued that a dimensional approach in which personality is described by individual specific traits, along which both normal and abnormal personality falls, may be favoured. This is supported by findings that interrater reliabilities are higher when assessing patients' characteristics of personality disorders with a dimensional task rather than with a categorical task (Clark, 1993). Additional advantages of the dimensional approach are that social dysfunction

measurements are continuously distributed; that similar patterns of correlations among traits are found in both personality-disordered and non-personality disordered individuals; and that sub-threshold personality disordered individuals are more akin to those experiencing the disorder rather than those who meet none of the criteria (Livesley et al, 1994). In the current case-control study, personality disorders revealed a clearer picture with respect to gender moderation in suicide completion among MDD participants, in comparison with personality predispositions represented by impulsive, hostile, and aggressive temperament and character traits. It could, thus, be argued that to understand the role of gender in fatal suicide, the syndromal approach is insightful. It will also be important, in further research, to delineate to what extent personality disorders correspond to deviations in personality traits.

One way of conceptualising our results is the following. On the one hand, in our male subsample, comorbidity between MDD and personality psychopathology (related to impulse-dyscontrol) is indicative of suicide completion. On the other hand, comorbidity between MDD and personality psychopathology is not indicative of suicide completion in the female subsample. This suggests that when men experience such comorbidity, they are more likely to respond with completing suicide. When women experience such comorbidity, however, they are more likely to avoid taking their lives. Many different causal chains may be related to this moderative effect of gender. Future studies might look into different possible

factors that may mediate this moderation. One such possibility is that psychosocial issues related to gender may predispose men more than women to respond with suicide completion when faced with depression-impulse dyscontrol comorbidity – the family environment, behavioural expectations, support networks, help-seeking behavioural habits may all conspire to succeed less in preventing suicide in men, rather than in women.

Another possibility is that the moderation of gender is merely a result of the temporal sequence between depression and impulsive personality deviations, of the two genders' differential exposure and experience with depression and Cluster B personality disorders. It may be that experiencing depression – an episodic disorder – leads to one developing coping strategies and building protective factors that are able to prevent suicide completion in the face of comorbidity with impulsive deviations. One reason for this could be that depression is often a debilitating and internalising experience, leading to more suffering in comparison to impulsivity, which may be more externalising and less subjectively impairing. Perhaps, then, when depressed women have impulsive tendencies, they have already developed some coping mechanisms, as a result of their experience potentially with several depressive episodes. To this extent, they would be more protected against suicide completions. On the other hand, when impulsive men experience depression, they may be lacking in the same coping mechanisms and more frequently come to complete suicide. This hypothesis rests on the assumption that Cluster B personality

and high impulsivity may be fluctuating, in time, in its potency to exacerbate the psychosocial impairment provided by depression. Previous knowledge accumulated in regards to the temporal and situational aspects of personality is now consistent with the idea that, within one individual, personality variables are consistent in time within the same situation, rather than across situations in at one particular time period. For this reason, then, one could imagine that a depressive episode may bring about situations that would render one person more impulsive than otherwise. Depression-related factors may in turn protect against severe reactions to such complications. If depression is more prevalent among women, it may be that a control outpatient sample of depressed women is more typical of depressed individuals than a male subsample, and explain (some of) the gender difference.

It could be tested experimentally whether or not the mere experience of depression leads to accumulating coping mechanisms and building protective factors. This might be done by employing a longitudinal design that assesses impulsive-related traits and pathology over time, along with depressive symptoms, their severity, and self-harm behaviour, as well as subjective assessments of perceived impairment resulting from their deviation. Moreover, one would need to assess whether the number of depressive episodes and the age of the first episode are mediators of the comorbidity – suicide completion relationship. It could also be explored whether this trend is indeed caused by comorbidity, rather than just a mere

artefact of having MD as a control condition, rather than personality psychopathology.

It is noteworthy that the trend in men is clear from the results in most of the variables we studied: six-months alcohol and six-month drug dependence, high impulsivity, Cluster B diagnosis, APD, BPD, gambling, and self-directedness. The trend in women, however, is not as clearly delineated, since we did get a significant SC odds ratio between those with and those without lifetime alcohol, as well as those with and those without lifetime drug dependence. It would be interesting to assess, in future studies, whether the chronicity of this substance dependence is related to depressive episodes, and if this relation mediates the effect of comorbidity on suicide completion. Conversely, one might try to determine whether current alcohol dependence without lifetime diagnosis coincides with first depressive episodes and their comorbidity with highly impulsive tendencies to affect SC odds.

According to the framework for *moderators* and *mediators* established by Baron and Kenny (1986), *moderation* is supported by a significant interaction effect between the moderator and an independent variable on an outcome (Baron & Kenny, 1986). To the extent that an analysis of variance assigning gender and suicidality group as predictors of temperament and character traits is appropriate to test moderation effects, our results would indicate that gender is a moderator of the link between suicide completion and novelty seeking (in the full factorial ANOVA), and of suicide completion and reward dependence (in the individual effects

ANOVA). On the other hand, to the extent that a logistic regression model predicting suicidality from gender and other variables is appropriate, we can conclude that gender is a moderator of the effect of Cluster B diagnosis on suicide completion, even after controlling for MDD, and adjusting for cluster A disorders, and previous suicide attempts. In other words, gender moderates the effect by a factor of 19: comorbidity of Cluster B and MDD in men is 19 times more predictive of suicide completion than in women.

This allows for the consideration of an interesting situation. Gender may be the moderator of the effect of MDD on suicide completion, of the effect of personality psychopathology on suicide completion, or, as shown in this study, of their comorbidity. Are these gender moderation processes the same? In other words, are they mediated by the same factor? Applying Baron and Kenny's (1986) concept of mediated moderation (Baron & Kenny, 1986), it would be interesting to discover whether there is one underlying factor for gender differences in Axis I and Axis II psychopathology determinants of suicide completion. While the *moderation* effect of gender may allow us to target suicide prevention approaches differentially for the two genders (especially in the context of personality-depression comorbidity), the *mediation-moderation* effect would allow for a more "dynamic conception", (Baron & Kenny, 1986, pp. 1181), in which the causal pathway underlying this moderation would be understood, and, as a result, the treatment of

depression, personality deviations and their comorbidity would be more satisfactorily attained in both genders.

In their discussion of *moderators* and *mediators*, Kraemer et al. (2001) recommend that researchers consider “stratifying samples by the strongest moderators and [...] further manipulations to the protocols for treatments are suggested by the mediators (Kraemer, et al., 2001, pp. 855). Taking into account the mediation-moderation considerations discussed above, it might be beneficial, in future studies, to also stratify samples by gender, and discover whether the mediating factors are different across genders.

To establish the moderating and mediating properties of risk factors, Kraemer et al. (2001) have proposed a method whereby one would establish the relative temporal precedence of risk factors, their (co)dominance, or potency in predicting the outcome, and whether or not they are correlated. Within this framework, risk factors that exhibit no temporal precedence, yet are correlated and codominant, are denoted as *overlapping risk factors*) (Kraemer, Stice, Kazdin, Offord, & Kupfer, 2001). Thus, impulsivity, hostility, APD, and BPD may all be considered potential overlapping risk factors. More importantly, in the Kraemer et al. (2001) model, moderators are uncorrelated with the other predictor, the moderator and the predictor codominate, and the moderator precedes the other predictor. Since gender is correlated to both depression, impulsive-aggressive traits and Cluster B personality, this framework would dismiss gender as a moderating

factor. Rather, depression might be considered a mediator of gender and suicide completion, if it was established that depression and gender are codominant, or that depression codominates gender. Future analyses might take this framework into consideration.

Acknowledging the difficulty in establishing precedence between two dimensional risk factors, both of which may vary within an individual over time, Kraemer et al. (2001) suggest, as a solution, defining a threshold along one such dimension and establishing when they are crossed in time (Kraemer, et al., 2001). An example of this could be the severity of a depressive episode and the trait of impulsivity. A longitudinal design, then would allow for delineating the relations between risk factors other than gender, on the causal pathway to suicide completion, as well as for indicating when interventions might be more or less effective.

As gender itself reveals the impact of social influences and societal change, cultural and religious heterogeneity in future samples may also be essential to build a bridge between psychopathology and psychosocial theories of gendered suicide. Moreover, future studies may build on the current methodological strength and adopt prospective analyses which could help elucidate the relationships between gender, depression, and its psychological comorbidities in their contribution to suicide completion. Clearly, understanding the role of gender in suicidal behaviour will be crucial towards improving sensitivity and specificity in predicting the most fatal outcome of major depressive disorder – suicide.

Chapter 4 CONCLUSION

The major finding among men was that depressed suicides differed from depressed controls in their likelihood of meeting the criteria for a Cluster B personality disorder, and for high impulsivity scores. Compared to depressed controls, depressed women suicides had a higher likelihood of lifetime substance dependence and higher hostility scores. After controlling for the effects of previous suicide attempts and Cluster A diagnosis, among individuals with MDD, gender significantly moderates the effect of having met the criteria for a Cluster B diagnosis.

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