Non-Suicidal Self-Injury in Adolescents:

Executive Functions and the Role of Serotonin in Impulsivity

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Contents

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List of Papers

1. Fikke, L. T., Melinder, A., & Landrø, N. I. (2011). Executive functions are impaired in adolescents engaging in non-suicidal self-injury. *Psychological Medicine, 41*, 601-610. doi:10.1017/S0033291710001030

2. Fikke, L. T., Landrø, N. I., & Melinder, A. (2010). Working Memory and Verbal Learning are Impaired in Adolescents Engaging in Non-Suicidal Self-Injury. (Under review).

3. Fikke, L. T., Melinder, A., & Landrø, N. I. (2011). Acute tryptophan depletion influences impulsivity but not mood in adolescents engaging in non-suicidal self-injury. (Under review).

List of Abbreviations

5-HT	5-Hydroxytryptamine, Serotonin
ADHD	Attention Deficit Hyperactivity Disorder
ANOVA	Analysis of Variance
ATD	Acute Tryptophan Depletion
BAI	Beck Anxiety Inventory
BDI	Beck Depression Inventory
BPD	Borderline Personality Disorder
CANTAB	Cambridge Neuropsychological Test Automated Battery
CAVLT-2	Children's Auditory Verbal Learning Test-2
CPT	Continuous Performance Test
CPT-IP	Continuous Performance Test, Identical Pairs Version
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th edition
DSM-V	Diagnostic and Statistical Manual of Mental Disorders, 5th edition
EF	Executive Functions
FASM	Functional Assessment of Self-Mutilation
FSIQ	Full-Scale Intelligence Quotient
IED	Intra/Extradimensional
IGT	Iowa Gambling Task
IQ	Intelligence Quotient
K-SADS-PL	Kiddie-Sads-Present and Lifetime Version
MDD	Major Depressive Disorder
MFF20	Matching Familiar Figures Test
NAD	Nicotine-adenine dinucleotide
NSD	Norwegian Social Science Data Services
NSSI	Non-Suicidal Self-Injury
PIQ	Performance Intelligence Quotient
POMS	Profile of Mood States
PTSD	Post-Traumatic Stress Disorder
SSRI	Selective Serotonin Reuptake Inhibitor
SSRT	Stop Signal Reaction Time
SST	Stop Signal Task
STAXI	State-Trait Anger Expression Inventory
SWM	Spatial Working Memory
TMD	Total Mood Disturbance
VIQ	Verbal Intelligence Quotient
WASI	Wechsler Abbreviated Scale of Intelligence

The Theme of this Thesis

In the last few decades, there has been an increased focus on non-suicidal self-injury in general and in adolescents in particular. Research findings show that non-suicidal self-injury is alarmingly widespread even in community samples of adolescents. Furthermore, non-suicidal self-injury is associated with psychological suffering, such as depression, suicidality, and anger problems, emphasizing the seriousness of this behaviour. However, little is known of underlying factors that can be involved in non-suicidal self-injury. In particular, research investigating the possible roles of neuropsychological and serotonin functions in non-suicidal self-injury in adolescents is scarce. One main aim of this dissertation was therefore to investigate various aspects of neuropsychological functions in adolescents engaging in non-suicidal self-injury. Another main aim was to investigate the effects of low serotonin function on impulsivity and mood in female adolescents engaging in non-suicidal self-injury. To examine these research aims, community sampled adolescents were recruited to participate in the study involving three sessions; a screening session, a test session and an experimental session. In the test session, a comparative cross sectional design was used to investigate neuropsychological functions in adolescents engaging in non-suicidal self-injury as compared with a healthy control group. In the experimental session a randomized double-blind placebo-controlled parallel group design was used. Specifically, the effects on impulsivity and mood of an experimentally induced lowering of serotonin, via acute tryptophan depletion, were investigated in female adolescents engaging in non-suicidal self-injury. The findings from this study could help illuminate various aspects of neuropsychological and serotonergic functioning that might be involved in non-suicidal self-injury in adolescents. In a theoretical perspective, the findings could yield knowledge about neuropsychological factors involved in non-suicidal self-injury, thereby contributing to the puzzle of understanding why adolescents

engage in non-suicidal self-injury, at least from a neuropsychological perspective. Also, the findings from the study could yield valuable knowledge about neuropsychological as well as serotonin functioning that should be targeted in applied and clinical settings to help adolescents discontinue engaging in non-suicidal self-injury as well as to reduce possible functional consequences of deficits in specific neuropsychological functions.

Introduction

Self-Injurious Behaviours

The phenomena of self-injury has existed for thousands of years. Acts of self-injury are described in the Old Testament in 3 Kings 18:28; " So they cried with a loud voice and cut themselves after their manner with knives and lancets till they were all covered with blood," as well as in the New Testament in Mark 5:5; "…and he was always day and night in the monuments and in the mountains crying and cutting himself with stones."

The field of self-injurious behaviours has been troubled by inconsistent terminology (Jacobsen & Gould, 2007; Muehlenkamp, 2005; Skegg, 2005). Numerous terms are used to refer to the various phenomena within the field (Muehlenkamp, 2005). Examples of these terms are: self-mutilation (Briere & Gil, 1998; Favazza, 1998), deliberate self-harm (Gratz, Conrad, & Roemer, 2002; Hawton, Rodham, Evans, & Weatherall, 2002), parasuicidal behaviour (Linehan, Armstrong, Suarez, Allmon, & Heard, 1991), self-injurious behaviour (Ohmann et al., 2008), non-suicidal self-injury (NSSI; Lloyd-Richardson, Perrine, Dierker, & Kelley, 2007), self-cutting (Hintikka et al., 2009) and self-inflicted injury (Jablonska et al., 2009). Importantly, different terms are used to refer to the same phenomena, whereas the same term is used to refer to different phenomena in various research groups (Jacobsen & Gould, 2007). For instance, in North America, "deliberate self-harm" refers to the deliberate, direct destruction or alteration of body tissue without suicidal intent (Gratz et al., 2002), whereas in the United Kingdom, "deliberate self-harm" refers to any deliberate self-injurious or self-poisoning act with a non-fatal outcome, regardless of suicidal intent (Hawton et al., 2002). Thus, several researchers (Hawton et al., 2002, 2003; Hurry, 2000) do not separate either 1) indirect from direct self-harm or 2) suicidal behaviours, i.e., behaviours engaged in

with the intent to die as a result of the acts, from self-injurious behaviours without suicidal intent.

NSSI refers to the deliberate, direct destruction or alteration of body tissue without conscious suicidal intent (Favazza, 1998; Lloyd-Richardson et al., 2007). NSSI is differentiated from indirect self-harm, such as overdose, drinking and driving and self-poisoning, and is socially unacceptable, as opposed to for instance ear piercing and professionally applied tattooing (Lloyd-Richardson et al., 2007; Walsh & Rosen, 1988). Examples of NSSI are cutting, carving, and burning skin, hitting self and picking at wounds (Favazza, 1998; Lloyd-Richardson et al., 2007).

Indeed, multiple lines of arguments and research findings suggest that NSSI is distinct and so should be differentiated from suicidal behaviours (Muehlenkamp, 2005). First, the obvious difference between NSSI and suicidal behaviours is the intent of the behaviours; NSSI is engaged in with no intent to kill oneself and thus is engaged in for reasons other than to end one's life, while suicidal behaviours are engaged in to kill oneself (O'Carroll et al., 1996; Simpson, 1980). Specifically, NSSI is often engaged in to alter one's general state of mind or consciousness, not to terminate consciousness as is the goal of engaging in suicidal behaviours (Walsh & Rosen, 1988). Second, individuals generally report feeling better *after* having engaged in NSSI, their state of mind is altered and their tension reduced, whereas in individuals committing suicide, whatever relief is to be gained is experienced *before* their suicidal act (Walsh & Rosen, 1988). Along these lines, individuals engaging in NSSI are most interested in what happens *after* having engaged in NSSI, whereas individuals committing suicide will never experience the results of their suicidal act alive (Walsh & Rosen, 1988). Relatedly, adolescents engaging in NSSI reported more positive attitudes towards life as compared with adolescents with previous suicide attempts (Muehlenkamp & Gutierrez, 2004).

Third, at the individual level NSSI typically is engaged in repetitively, involves the use of

several methods and consists of low-lethality behaviours (Simpson, 1980; Walsh & Rosen,

1988). This contrasts with suicidal behaviours which at the individual level typically occur

infrequently, do not involve the use of multiple methods and involve high lethality (Walsh &

Rosen, 1988). Fourth, NSSI differs from suicidal behaviours with respect to demographic

characteristics (see Muehlenkamp, 2005, for a review). NSSI is more prevalent than suicide

attempts and completed suicide combined. Also, NSSI is more prevalent in adolescence,

while completed suicide is more common in adults (Muehlenkamp, 2005). Furthermore,

several findings show similar prevalence rates of NSSI in boys and girls (Garrison et al.,

1993; Muehlenkamp & Gutierrez, 2004; Zoroglu et al., 2003, but see Laye-Gindhu &

Schonert-Reichl, 2005; Muehlenkamp & Gutierrez, 2007; Ross & Heath, 2002), while

completed suicides are more common in males, at least in the Western part of the World (see

Gould, Greenberg, Velting, & Shaffer, 2003, for a review). In sum, these arguments and

findings supporting considerable differences between NSSI and suicidal behaviours should

not be overlooked. They implicate that different prevention and treatment efforts are needed

with respect to NSSI and suicidal behaviours, respectively (Muehlenkamp, 2005).

Non-Suicidal Self-Injury

In one classification scheme, NSSI is divided into three main categories based on

degree of tissue destruction and the rate and pattern of behaviour (Favazza, 1998). Major self-

injury involves dramatic and extreme albeit infrequent acts such as autocastration, self-

enucleation and limb amputation (Favazza, 1998; Stanley, Winchel, Molcho, Simeon, &

Stanley, 1992) and is most often associated with psychosis and acute intoxications (Favazza,

1998; Jacobsen & Gould, 2007). Individuals often explain their acts of major self-injury with

reference to religious and/or sexual themes such as spiritual purification, punishment for sins,

response to heavenly commands and visions and rescission of troublesome genitals (Favazza, 1998).

Stereotypic self-injury are often repetitive and sometimes rhytmic and refers to acts such as head banging, hitting and self-biting (Favazza, 1998; Stanley et al., 1992). Stereotypic self-injury is engaged in by individuals with Lesch-Nyhan syndrome, mental retardation, and/or pervasive developmental disorders such as autism (Favazza, 1998; Jacobsen & Gould, 2007; Nyhan, 2005; Stanley et al., 1992).

Superficial/moderate self-injury can be subdivided into the compulsive and the episodic types, respectively (Favazza, 1998). Compulsive superficial/moderate self-injury involves acts such as skin picking and trichotillomania (Favazza, 1998). Indeed, findings implicate partly overlapping neurobiological underpinnings to trichotillomania (compulsive hair pulling) and obsessive-compulsive disorder (Chamberlain, Fineberg, Blackwell, Robbins, & Sahakian, 2006). Episodic superficial/moderate self-injury refers to acts such as skin cutting, carving and burning (Favazza, 1998). When self-injuring acts of the episodic type become an overwhelming preoccupation, episodic becomes repetitive self-injury (Favazza, 1998). However, there are no clear cut objective, observable criteria defining "overwhelming preoccupation." The switch from episodic to repetitive self-injury is indeed described as "fluid" (Favazza, 1998). For purposes of the present research project, we focused exclusively on NSSI occurring as episodic/repetitive superficial/moderate self-injury. Thus, in the following we refer exclusively to this category of NSSI when using the term "NSSI".

Until at least quite recently, engaging in NSSI has been associated mainly with individuals with personality disorders, especially borderline personality disorder (BPD; Stanley et al., 1992; Zanarini, Gunderson, Frankenburg, & Chauncey, 1990). Indeed, recurrent suicidal behaviour, gestures, or threats, or self-mutilating behaviour is one of the criteria for a

diagnosis of BPD in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV; American Psychiatric Association, 1994). However, recent research findings show that community sampled as well as outpatient and inpatient adolescents and young adults with a history of NSSI are a heterogeneous group with respect to psychiatric symptoms and diagnoses (Hintikka et al., 2009; Jacobsen, Muehlenkamp, Miller, & Turner, 2008; Nock, Joiner, Gordon, Lloyd-Richardson, & Prinstein, 2006; Nock & Mendes, 2008). In addition, a considerable number of them does not meet criteria for any axis I DSM-IV diagnoses, such as with 12% of inpatient adolescents (Nock et al., 2006) and 21% of community sampled adolescents (Hintikka et al., 2009). Accordingly, it has been suggested that NSSI should be an independent, distinct axis I diagnosis as an impulse control disorder (Favazza, 1998), as a deliberate self-injury syndrome (Muehlenkamp, 2005) or as a deliberate self-harm syndrome, characterized by multiple recurrent episodes of low lethality self-harm deliberately inflicted upon the body (Pattison & Kahan, 1983). Indeed, NSSI is proposed as a separate diagnostic category in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-V; American Psychiatric Association, 2010).

NSSI is alarmingly widespread in adolescents. As many as 61% of adolescent psychiatric inpatients reported ever having engaged in NSSI (DiClemente, Ponton, & Hartley, 1991). Indeed, in a recent study, 82% of adolescent psychiatric inpatients had engaged in NSSI during the previous 12 months (Nock & Prinstein, 2004). Even in community samples of adolescents, lifetime prevalence rates of NSSI range from 14% - 23% (Muehlenkamp & Gutierrez, 2004, 2007; Ross & Heath, 2002; Zoroglu et al., 2003). Furthermore, in young community adolescent girls, 56% reported having engaged in NSSI during their lifetime (Hilt, Cha, & Nolen-Hoeksema, 2008). During a 12-month period, as many as 46% of community sampled adolescents reported having engaged in NSSI (Lloyd-Richardson et al., 2007). It has

been speculated whether prevalence rates of NSSI among community sampled adolescents are increasing (Jacobsen & Gould, 2007). However, findings based on data from 2001 to 2005 suggest that although overall lifetime rates of NSSI among community sampled adolescents may fluctuate across years, they generally have remained consistent (Muehlenkamp, Williams, Gutierrez, & Claes, 2009). Equal prevalence rates in NSSI between females and males were found during the first 3 years. However, during the last 2 years of the study, the rate of NSSI among females increased significantly, whereas males' rates of NSSI declined (Muehlenkamp et al., 2009). Relatedly, there are mixed findings with respect to sex-differences in prevalence rates of NSSI. In adolescent psychiatric patients, Nock and Prinstein (2004) found no sex-difference in prevalence rates of NSSI, whereas Jacobsen et al. (2008) found that females are more likely to engage in NSSI as compared with males. Likewise, in community sampled adolescents, some find a higher prevalence rate in females than in males (Laye-Gindhu & Schonert-Reichl, 2005; Muehlenkamp & Gutierrez, 2007; Ross & Heath, 2002), whereas others find no such sex-difference (Garrison et al., 1993; Muehlenkamp & Gutierrez, 2004; Zoroglu et al., 2003). Onset of NSSI behaviours is typically reported to be between 12 and 14 years of age in both community sampled adolescents (Muehlenkamp & Gutierrez, 2007; Ross & Heath, 2002) and in adolescent psychiatric inpatients (Nock & Prinstein, 2004).

NSSI is a heterogeneous phenomenon, ranging from minor to severe forms (Lloyd-Richardson et al., 2007). Cutting, scratching and self-hitting were among the top four methods used to self-injure in community sampled adolescents (Laye-Gindhu & Schonert-Reichl, 2005; Muehlenkamp & Gutierrez, 2004, 2007; Ross & Health, 2002). Similarly, cutting, picking at a wound, scraping and self-hitting were among the most common methods used to self-injure in clinical adolescent samples (Guertin, Lloyd-Richardson, Spirito, Donaldson, &

Boergers, 2001; Nock & Prinstein, 2004). Whether all behaviours that qualify for NSSI according to the definition are of clinical significance are unresolved issues (Lloyd-Richardson et al., 2007). For instance, picking at a wound may in isolation reflect non-pathological, non NSSI (Lloyd-Richardson et al., 2007), suggesting that engaging in behaviours that meet the criteria for NSSI might not in iself be of clinical significance. Nevertheless, it appears that those who are engaging in several NSSI behaviours also are picking at wounds, in a self-injuring way, as opposed to benign picking at a scab etc. (E. E. Lloyd-Richardson, personal communication, October 10, 2007). Exploring why the particular adolescent engages in NSSI behaviours and thoroughly assessing associated psychological suffering might be some of the relevant factors when examining whether NSSI behaviours are of clinical significance for the individual adolescent.

It has been suggested to classify NSSI behaviours into three groups based on their potential for causing tissue damage (Skegg, 2005; Whitlock, Muehlenkamp, & Eckenrode, 2008). The first group includes behaviours with the potential for superficial tissue damage, such as scratching until marks remain on the skin or bleeding occurs. Behaviours that often cause bruising or light tissue damage, such as punching oneself or other objects, are encompassed in the second group. The third group includes behaviours that likely cause severe tissue damage, such as cutting, carving or burning areas of the body (Whitlock et al., 2008). The three groups of NSSI behaviours reflect increasingly severe forms of NSSI (Whitlock et al., 2008). Supporting this classification, NSSI forms as categorized into one of the three groups, was one important characteristic in classifying individuals engaging in NSSI, into different subgroups (Whitlock et al., 2008). Although the picture is not completely consistent (Nock & Prinstein, 2004), some find sex differences in the forms of NSSI engaged in in adolescents and young adults (Whitlock et al., 2008). For instance, in community

sampled adolescents, males were more likely to engage in self-battery, whereas females were more likely to report cutting and severe scratching (Muehlenkamp, Yates, & Alberts, 2004 as cited in Whitlock et al., 2008).

NSSI is associated with a range of psychiatric symptoms and diagnoses. In inpatient adolescents having engaged in NSSI in the previous 12 months, 88% met criteria for at least one DSM-IV axis I diagnosis (Nock et al., 2006). Specifically, 42% met criteria for major depressive disorder (MDD), 24% met criteria for post-traumatic stress disorder (PTSD), 16% met criteria for generalized anxiety disorder, 50% met criteria fror conduct disorder, 45% met criteria for oppositional defiant disorder and 60% met criteria for any substance use disorder. Likewise, Jacobsen et al. (2008) found elevated rates of MDD (46%), dysthymia (28%), PTSD (6%), any anxiety disorder (32%), any eating disorder (8%), any disruptive behaviour disorder (33%) and any substance use disorder (7%) among outpatient adolescents with a recent history of NSSI. Even in adolescent community samples, NSSI is associated with expressions of psychological distress, such as elevated levels of depressive (Laye-Gindhu & Schonert-Reichl, 2005; Ross & Heath, 2002) and anxious symptoms (Ross & Heath, 2002) and anger control problems (Laye-Gindhu & Schonert-Reichl, 2005). Also in community sampled adolescents, NSSI is associated with MDD (Garrison et al., 1993; Hintikka et al., 2009), anxiety disorders (Garrison et al., 1993; Hintikka et al., 2009) and eating disorders (Hintikka et al., 2009). Furthermore, NSSI is associated with suicide ideation (Garrison et al., 1993; Laye-Gindhu & Schonert-Reichl, 2005; Lloyd-Richardson et al., 2007), suicide plans (Laye-Gindhu & Schonert-Reichl, 2005) and suicide attempts (Laye-Gindhu & Schonert-Reichl, 2005; Lloyd- Richardson et al., 2007) in community samples of adolescents. Indeed, as many as 70% of adolescent psychiatric inpatients engaging in NSSI reported a lifetime history of at least one suicide attempt (Nock et al., 2006).

Overall, 67% of the female inpatient adolescents in the study by Nock et al. (2006) met the criteria for a DSM-IV personality disorder. Although about half of the female participants (52%) met criteria for BPD, a considerable amount of them also met criteria for avoidant (31%) and paranoid (21%) personality disorders, respectively (Nock et al., 2006). Anyhow, diagnosing personality disorders in adolescence is controversial (Jacobsen & Gould, 2007). On the one hand, adolescence is a time of rapid change and development, and personality disorders show substantial instability in adolescence (Mattanah, Becker, Levy, Edell, & McGlashan, 1995). Thus, signs of personality disorders in adolescents may accurately reflect current distress and dysfunction but they may not represent coherent, differentiable syndromes with stability over time (Becker, Grilo, Edell, & McGlashan, 2000). On the other hand, by ignoring possible personality disorders in this age group, many adolescents may not receive appropriate psychological treatments (Miller, Muehlenkamp, & Jacobsen, 2008). Indeed, some findings show that features of some personality disorders have construct validity and can be reliably identified in adolescents (Ludolph et al., 1990).

Little is known of the underpinnings of NSSI (Lloyd-Richardson et al., 2007). Some etiological factors are probably childhood trauma such as physical, emotional and sexual abuse, neglect and separation (Gratz et al., 2002; Zorouglu et al., 2003), insecure attachment (Gratz et al., 2002), dissociation (Gratz et al., 2002; Zoruglu, et al., 2003), undesirable life events (Garrison et al., 1993) and biological vulnerabilities involving noradrenergic, serotonergic, doperminergic and opiatergic abnormalities (Oquendo & Mann, 2000; Stanley et al., 1992).

Research findings suggest a role for impulsivity in NSSI. Impulsivity can be defined as the failure to resist an impulse, drive or temptation that is harmful to onself or others (Cherkasky & Hollander, 1997). A majority of adolescents reports that their NSSI typically is

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engaged in impulsively or with little forethought (Kumar, Pepe, & Steer, 2004; Lloyd-Richardson et al., 2007; Nock & Prinstein, 2005). Also, NSSI is associated with heightened levels of self-reported impulsivity (Ross, Heath, & Toste, 2009). Furthermore, lifetime frequency of NSSI is positively correlated with impulse regulation difficulties (Ross et al., 2009). However, these findings are exclusively based on self-reports. People may have only little or no direct introspective access to higher order mental processes, such as those involved in the initiation of behaviour (see Nisbett & Wilson, 1977, for a review). Thus, one might question the accuracy of the adolescents' subjective reports about impulsivity.

To address the question of why adolescents engage in NSSI, Nock and Prinstein (2004) proposed a model of the functional processes that produce and maintain NSSI behaviours. The model includes four primary functions of NSSI differing along two dichotomous dimensions. First, NSSI is engaged in because it is automatically reinforcing (e.g., to regulate emotions) and/or socially reinforcing (e.g., to regulate or alter one's social environment). Second, NSSI is engaged in because it is reinforced in a positive (i.e., followed by a favorable stimulus) or negative manner (i.e., followed by the removal of an aversive stimulus) (Nock & Prinstein, 2004). Automatic-negative reinforcement refers to engaging in NSSI to reduce negative affective states ("to stop bad feelings"). Automatic-positive reinforcement involves engaging in NSSI to generate a desirable psychological state ("to feel something"). Social-negative reinforcement refers to engaging in NSSI to avoid or escape from interpersonal task demands ("to avoid doing something unpleasant"). Social-positive reinforcement involves engaging in NSSI to gain attention from others or gain desirable materials ("to let others know how unhappy I am") (Nock & Prinstein, 2004).

Adolescents typically report several reasons for engaging in NSSI (Lloyd-Richardson et al., 2007). A considerable number of both adolescent psychiatric patients (Nock &

Prinstein, 2004) and community sampled adolescents (Lloyd-Richardson et al., 2007) endorse social-reinforcement functions of their NSSI. Although not completely consistent (Lloyd-Richardson et al., 2007), reasons related to automatic reinforcement are nevertheless endorsed most frequently both by adolescent psychiatric patients (Kumar et al., 2004; Nock & Prinstein, 2004; Penn, Esposito, Schaeffer, Fritz, & Spirito, 2003) and community sampled adolescents engaging in NSSI (Laye-Gindhu & Schonert-Reichl, 2005; Ross & Heath, 2003). For instance, prior to engaging in NSSI, adolescents experience negative emotions, such as anger, sadness and anxiety, which are reduced during and especially after having self-injured (Laye-Gindhu & Schonert-Reichl, 2005; Ross & Heath, 2003). In sum, the bulk of the research findings supports the emotion regulation hypothesis, stating that adolescents engage in NSSI to regulate emotions, most often to decrease their negative affective states but sometimes also to generate affective states (Jacobsen & Gould, 2007). However, these findings are exclusively based on adolescents' retrospective self-reports, which might be questioned from a methodological perspective (Jacobsen & Gould, 2007). First, the retrospective nature of the self-reports, asking the adolescents why they engaged in NSSI several weeks or even months earlier, might be a threat to the reliability of the reports (Jacobsen & Gould, 2007). Second, self-reports depend on the adolescents having enough insight to consciously being aware of why they engage in NSSI (Jacobsen & Gould, 2007). As referred to above, a majority of adolescents report that their NSSI typically is engaged in impulsively or with little forethought (Kumar et al., 2004; Lloyd-Richardson et al., 2007; Nock & Prinstein, 2005), suggesting that a substantial number of them might not be aware of why they engage in NSSI.

Executive Functions in Emotion Regulation

Executive functions may be defined as the skills that are essential for purposeful, goal-directed activity (Anderson, 1998). Converging evidence indicates that the prefrontal cortex is central in executive functions (see Rogers et al., 2004, for a review). Although the different executive functions are interrelated, they are meaningfully diverse abilities (Miyake et al., 2000). Shifting between mental sets or tasks, updating and monitoring of information in working memory, and inhibition of dominant responses, are main aspects of executive functions (Miyake et al., 2000). Although the picture is not completely consistent (Herba, Tranah, Rubia, & Yule, 2006), some find sex differences in executive functions in adolescents (Anderson, Anderson, Northam, Jacobs, & Catroppa, 2001; Fields, Collins, Leraas, & Reynolds, 2009). For instance, females performed generally better than males on tests measuring set-shifting ability in a cross-sectional study investigating the development of this ability from childhood into early adulthood (Kalkut, Han, Lansing, Holdnack, & Delis, 2009). However, females and males showed differential developmental trajectories across ages. Females showed a faster rate of improvement than males on a design fluency switching task during adolescence until the 16-17 years age group at which point males' performance became greater than females'. On the other hand, on colour-word interference and verbal fluency switching tasks, males showed a faster rate of improvement during early adolescence than females (Kalkut et al., 2009).

In an empirically based model of the neural basis of emotion processing, two neural systems underlie neuropsychological processes that are important for emotional behaviour (Phillips, Drevets, Rauch, & Lane, 2003). The ventral system, including the amygdala, insula, ventral striatum and ventral regions of the anterior cingulate gyrus and prefrontal cortex, is primarily important for the identification of the emotional significance of a stimulus, the

ensuing production of an affective state, and the automatic regulation of emotional responses. The dorsal system includes the hippocampus and dorsal regions of anterior cingulate gyrus and prefrontal cortex. It is important for the performance of executive functions, which includes effortful regulation of affective states and emotional behaviours. This involves an inhibition or modulation of the processes that are mainly dependent upon the ventral system (Phillips et al., 2003).

In accordance with this model, multiple lines of research findings suggest that executive functions are relevant for emotion regulation. Several studies show that executive functions are impaired in disorders characterized by abnormalities in emotion regulation, such as depression (Harvey et al., 2004; see Rogers et al., 2004, for a review; Weiland-Fiedler et al., 2004) and bipolar mood disorder (see Bearden, Hoffman, & Cannon, 2001, for a review; Borkowska & Rybakowski, 2001). Furthermore, research findings show that individuals lower in working memory capacity struggle more than others in regulating both their emotional experiences and expressions (Schmeichel, Volokhov, & Demaree, 2008). By loading working memory with tasks demanding effortful cognitive processing, mood-congruent processing can be prevented and thereby result in distraction from negative moods (Van Dillen & Koole, 2007). In this way working memory is one mechanism through which distraction from negative moods operates (Van Dillen & Koole, 2007) and is thereby related to emotion regulation. Another mechanism through which emotion regulation occurs, is suppression (Nash et al., 2007). Although suppression does not provide relief from the subjective experience of negative emotions, it can be adaptive by restraining emotional expressive behaviours (Gross & Levenson, 1997). Specifically, unregulated emotional expression and responding might have destructive effects, as in the abrupt expression of anger, suggesting that in some circumstances the failure of withholding emotional expressions

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might be problematic (Gross & Levenson, 1997). Importantly, suppression demands inhibition of prepotent responses (Nash et al., 2007). Summing up, several lines of research findings implicate that impaired executive functions might suggest an ineffective ability *per se* to regulate emotions as well as emotional expressive behaviours.

The Neuropsychology of Self-Injurious Behaviours in General and NSSI in Particular

Only a few studies have examined neuropsychological functions in adolescents engaging in self-injurious behaviours in general and NSSI in particular. To a large extent the studies are based on the hypothesis that self-injurious behaviours may be associated with frontal lobe function. Accordingly, the studies have primarily investigated neuropsychological functions assumed to depend heavily on the frontal brain lobes. With one exception (Oldershaw et al., 2009), no deficits in the investigated neuropsychological functions have been found in adolescents engaging in self-injurious behaviours as compared with different comparison groups (Dougherty et al., 2009; Janis & Nock, 2009; Ohmann et al., 2008).

Examining social and emotional self-regulation in adolescent females engaging in self-injurious behaviours, no differences were found between adolescent females engaging in self-injurious behaviours and adolescent females with none such behaviours on tests of executive functions, i.e., the Stroop and the Wisconsin Card Sorting Test (Ohmann et al., 2008). No differences were found between adolescents and adults engaging in NSSI as compared to controls on behavioural measures of three different dimensions of impulsivity, i.e., the Conners' Continuous Performance Test (CPT), the Iowa Gambling Task (IGT) and a computer-based measure of delay discounting (Janis & Nock, 2009). In contrast, Oldershaw et al. (2009) found that adolescents who currently self-harmed, showed impaired decision making, as measured by the IGT, as compared with adolescents with a previous history of self-harm, adolescents with a depression and healthy controls. However, adolescents who

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currently or previously self-harmed were not impaired on the Means-Ends Problem-Solving

Procedure, a measure of problem-solving skills (Oldershaw et al., 2009). As compared with

adolescents with a history of at least one suicide attempt and of NSSI behaviours, adolescents

with a history of NSSI only did not show elevated levels of impulsivity, as measured by the

Two Choice Impulsivity Paradigm and the GoStop Impulsivity Paradigm, measuring two

different dimensions of impulsivity (Dougherty et al., 2009).

Several methodological issues should be considered when reviewing these studies.

First, as evident when referring to the studies, different terms involving different definitions

of self-injurious behaviours have been used across studies. In two of the studies (Ohmann et

al., 2008; Oldershaw et al., 2009), a broader definition of self-injurious behaviours, than that

of NSSI, was used. Specifically, the definition included direct and indirect forms of self-

injuring behaviours with and without suicidal intent. Also, in one of the studies (Dougherty et

al., 2009), any direct or indirect non-fatal self-injuring act that was committed without

suicidal intent, was included in the definition of NSSI. Thus, as the studies have used different

definitions of self-injurious behaviours, they have not investigated the exact same phenomena.

This illuminates the parcity of studies investigating neuropsychological functions exclusively

in adolescents engaging in NSSI. Second, some of the adolescents in the self-injuring groups

and/or the comparison groups were drawn from clinical populations in all four studies

(Dougherty et al., 2009; Janis & Nock, 2009; Ohmann et al., 2008; Oldershaw et al., 2009).

Thus, different comorbid conditions in both the self-injuring and the comparison groups in the

studies might have influenced the findings, making it difficult to detect potential specific

impairments in neuropsychological functions in adolescents engaging in self-injurious

behaviours. Third, all of the studies only had one group of adolescents engaging in self-

injurious behaviours. As adolescents engaging in self-injury represent a heterogeneous group

(Lloyd-Richardson et al., 2007; Whitlock et al., 2008), potential differences between subgroups of adolescents engaging in these behaviours and healthy controls, respectively, might be impossible to detect when treating all adolescents engaging in self-injury as one group. Fourth, to a considerable extent, the studies have used different tests of executive functions, impulsivity, decision-making and problem-solving. Even though all tests used in the studies are assumed to measure frontal lobe functions, they measure subtly different aspects of frontal lobe functions and by no means they capture all neuropsychological functions subserved by the frontal lobes. This emphasizes the need for conducting further studies investigating a broader range of neuropsychological functions depending both on the frontal lobes as well as on other brain structures, before establishing firm conclusions with respect to the neuropsychological functioning of adolescents engaging in NSSI. For instance, no previous studies have investigated verbal learning and memory in adolescents engaging in NSSI.

In addition to these methodological considerations, yet another issue might be relevant when considering the scarcity of neuropsychological findings supporting an association between self-injurious behaviours and impulsivity in particular. Conceivably, adolescents engaging in NSSI are impulsive only in certain contexts (Janis & Nock, 2009). It might be that they impulsively engage in NSSI only when under extreme stress or in psychological distress (Janis & Nock, 2009). Possibly, this might help explain why the majority of the reviewed neuropsychological studies using performance-based measures of impulsivity have not found elevated levels of impulsivity in adolescents engaging in self-injurious behaviours.

Serotonin in Self-Injurious Behaviours, NSSI, Emotion Regulation and Impulsivity

Although the picture is not completely consistent (Stanley et al., 2010), multiple lines of evidence suggest that serotonin (5-hydroxytryptamine, 5-HT) is implicated in the pathophysiology of self-injurious behaviour (McCloskey, Ben-Zeev, Lee, Berman, & Coccaro, 2009a). Decreased 5-HT activity has been linked to self-harm in general (Steiger et al., 2001) and NSSI in particular (Herpertz, Sass, & Favazza, 1997). Furthermore, selective serotonin reuptake inhibitor (SSRI) has proven effective in reducing self-injury (Markovitz, Calabrese, Schulz, & Meltzer, 1991). In adults with intermittent explosive disorder and in healthy controls, experimentally lowered 5-HT enhanced self-injurious behavior, assessed by a behavioural measure of self-aggression (McCloskey et al., 2009a). Peripheral serotonin levels were lower in adolescents engaging in self-inflicted injury as compared with healthy controls (Crowell et al., 2008). Again, different terms and definitions of self-injurious behaviours are used in the studies. For instance, in three of the studies, self-injurious behaviours encompassed both direct and indirect self-injurious acts with and without suicidal intent (Crowell et al., 2008; McCloskey et al., 2009a; Steiger et al., 2001). This emphasizes the need for further studies to investigate the association between serotonin functioning and NSSI in particular. Still, the findings might suggest a role for serotonin in self-injurious behaviours in general and NSSI in particular.

In addition to being associated with self-injurious behaviours in general and NSSI in particular, reduced 5-HT neurotransmission plays an important role in impaired emotion regulation (Canli & Lesch, 2007; Lesch, 2005; Walderhaug et al., 2007) as well as in impaired impulse control (Dolan, Anderson, & Deakin, 2001; Linnoila et al., 1983; Walderhaug et al., 2002, 2007). Indeed, abnormalities in 5-HT function in regions of the prefrontal cortex may be especially important in impaired emotion regulation resulting in impulsive affective action

(Davidson, Putnam, & Larson, 2000). Possibly, the mechanism for the association between NSSI, impaired emotion regulation, and the potential heightened level of impulsivity might be found in lowered 5-HT function.

There are various subtypes of impulsivity (Evenden, 1999; Schmidt, 2003; Winstanley, Dalley, Theobald, & Robbins, 2004), such as dimensions of impulsive action, or the inability to inhibit a prepotent motor response or behavioural disinhibition (McCloskey et al., 2009b; Winstanley et al., 2004), and cognitive impulsivity (McCloskey et al., 2009b; Schmidt, 2003), such as reflection impulsivity (Morgan, Impallomeni, Pirona, & Rogers, 2005), impulsive decision making and impulsive choice (Winstanley et al., 2004). Low 5-HT function seems particularly closely associated with increased impulsivity on behavioural measures reflecting the dimension of impulsive action (Crean, Richards, & de Wit, 2002; Walderhaug et al., 2002, 2007; Winstanley et al., 2004, but see Clark et al., 2005). NSSI is associated with low 5-HT function, which in turn is closely linked to increased impulsive action. Thus, NSSI might appear as a type of impulsive action rather than involving a type of cognitive impulsivity.

Main Research Aims

Paper I

A primary aim of the study was to explore the main aspects of executive functions, i.e., shifting, updating and inhibition, in adolescents engaging in NSSI. As adolescents engaging in NSSI constitute a heterogeneous group, we examined a high-severity NSSI group, a low-severity NSSI group in addition to a control group along these basic dimensions of executive functions. As there may be sex differences in NSSI and executive functions, we investigated the possible interactive of sex.

Paper II

Another main aim of the study was to explore verbal learning, recall, recognition and intrusions in adolescents engaging in NSSI as compared with healthy controls. As females outperform males in verbal learning and memory, we investigated the interactive effect of sex.

Paper III

The primary aims were to investigate the effects of an experimentally induced lowering of serotonin, via acute tryptophan depletion (ATD), on impulsivity and mood in female adolescents engaging in NSSI. It was hypothezised that the tryptophan-depleted girls would show increased impulsive action and report lowered mood as compared with their sham-depleted counterparts.

Materials and Methods

Design

The study consisted of three different sessions; a screening session, a test session and an experimental session. In the test session, a comparative cross sectional design was used. Neuropsychological functioning and clinical characteristics were assessed in adolescents engaging in NSSI as compared with healthy controls. In the experimental session involving ATD, a randomized double-blind placebo-controlled parallel group design was used. Female adolescents engaging in NSSI were randomly assigned to either a tryptophan or a sham depletion group, respectively. Performance on measures of impulsivity and mood was compared between the respective tryptophan-depleted and sham-depleted female adolescents. Neither the experimenters nor the participants were aware of the participants' group status.

Participants and Procedures

The data included in the three papers in this thesis was collected from the same pool of participants. The data reported and discussed in papers I and II was collected from the sample selected from the screening session. The data reported and discussed in paper III was collected from adolescents who were selected from the screening session and who had participated in the test session. In paper I, data from 97 participants was included, in paper II, data from 98 participants were included and in paper III, data from 32 participants were included.

See figure 1 for the description of the participants in the three sessions of the study.

Figure 1. The participants in the three sessions of the study

| 17 high schools in Oslo and nearby boroughs agreed to participate |
| 327 adolescents were recruited and participated in the screening session |
| 74 adolescents in the NSSI group and 42 adolescents in the control group were selected for participation in the test session |

Adolescent opt out in NSSI group (n=12)
Adolescent opt out in control group (n=1)

62 adolescents (48 females, 14 males) in the NSSI group and 41 adolescents (30 females, 11 males) in the control group participated in the test session

Paper I and paper II: 5 adolescents (4 females, 1 male) in the control group excluded from all data analyses
Paper I: 1 additional adolescent (female) in the control group excluded from all data analyses

Paper I : NSSI group (n=62; 48 females, 14 males) and control group (n= 35; 25 females, 10 males)
Paper II: NSSI group (n=62; 48 females, 14 males) and control group (n= 36; 26 females, 10 males)

42 female adolescents in the NSSI group were convenience sampled for participation in the experimental session

Adolescent opt out (n=2)
Parental opt out (n=1)
Adolescents excluded from participation because of SSRIs (n=2)

37 female adolescents in the NSSI group participated in the experimental session

Adolescents excluded from analyses because of vomiting (n=4)
Adolescents excluded from analyses because of refusing to ingest the mixture (n=1)

32 female adolescents in the NSSI group were included in all data analyses from the experimental session (Paper III)

Seventeen high schools in Oslo and nearby areas agreed to participate in the study. All Grade 9 students present at the schools at the scheduled times, were approached to participate via classroom announcements. As will be described, one group of participants were seen only in the screening session, a second group in the screening and test sessions, and a third group in the screening, test and experimental sessions.

The screening session. A total of 327 adolescents were recruited and participated in the screening session. Participants from each school completed a questionnaire on NSSI in a classroom. NSSI was defined as the deliberate, direct destruction or alteration of body tissue without suicidal intent. This excludes acts such as mentally hurting oneself and engaging in risky behaviours. Inclusion in the NSSI group required having engaged in at least two

different NSSI behaviours during the past year, as assessed by their responses on the questionnaire on NSSI. Group sizes of approximately 30 adolescents would enable us to detect group differences in neuropsychological functions (Kyte, Goodyer, & Sahakian, 2005; Matthews, Coghill, & Rhodes, 2008). To ensure such group sizes in the ensuing test session, we screened until we had 74 adolescents meeting the criteria for inclusion in the NSSI group. The control group comprised 42 adolescents matched as closely as possible on sex, ethnicity and school belonging to the NSSI group, and had never engaged in any NSSI.

The test session. Ahead of the test session, 12 of the 74 adolescents in the NSSI group and 1 of the adolescents in the control group withdrew from further participation. This left 62 adolescents *(48 females, 14 males; typical age range 14-15 years)* in the NSSI group and 41 adolescents *(30 females, 11 males; typical age range 14-15 years)* in the control group in the test session. All participants met at the Department of Psychology at the University of Oslo. They completed neuropsychological tests and questionnaires on clinical characteristics. A clinical psychologist administered the sections covering some selected psychiatric diagnoses in a semi-structured diagnostic interview. All participants were tested individually. Five participants who had reported they had never engaged in NSSI on the screening questionnaire, revealed in the interview that they had engaged in one NSSI behaviour during the past year. They were excluded from all analyses as they failed to meet the criteria for any of the groups, this left 36 adolescents (*26 females, 10 males; typical age range 14-15 years*) included in the control group. Due to extreme scores on several measures on the executive functions tests, one girl in the control group was excluded from all the analyses as reported in paper I.

With respect to all analyses as reported in paper I, based on participants' reported NSSI in the screening questionnaire and in the section on NSSI in the diagnostic interview, participants were classified into three groups: a high-severity NSSI group (*n*=33), a low-

severity NSSI group (*n*= 29) and a control group (*n*=35). Participants meeting the initial

criteria for inclusion in the NSSI group, were given a score reflecting the severity of their

NSSI. Two NSSI characteristics were used to calculate the NSSI severity score; *the form(s)*

and *the total number of different NSSI behaviours* engaged in. With respect to NSSI forms,

NSSI behaviours were classified into three groups based on their potential for causing tissue

damage (Skegg, 2005; Whitlock et al., 2008). Behaviours with potential for superficial tissue

damage were each scored 1, while those with potential for causing bruising or light tissue

damage were each scored 2. Lastly, behaviours with potential for causing severe tissue

damage, were each scored 3. To ensure reliability of the classification of NSSI behaviours

into the three groups, training of two raters was completed, resulting in 90% agreement on

20% of the data. Thus, for each participant meeting the initial criteria for inclusion in the

NSSI group, the weighted scores of the NSSI behaviours were summarized to give a NSSI

severity score (M=7.9, S.D.=3.6, Median=7.0). The median was used as the cut off point

separating the participants into the two NSSI subgroups. Nine participants scored this value.

Five were classified into the high-severity NSSI group as they had engaged in NSSI

behaviours in all three NSSI groups, a similar pattern to the majority (i.e., 25 of 28) of

participants in the high-severity NSSI group. The four remaining participants were classified

into the low-severity NSSI group as they had engaged in NSSI behaviours in two NSSI

groups, either group 1 and 2 or group 1 and 3, a similar pattern to the majority (i.e., 20 of 25)

of participants in the low-severity NSSI group.

   The experimental session. Inclusion in the experimental session (involving ATD)

required that the female adolescents had engaged in minimum two different NSSI behaviours

during the past year. Forty-eight female adolescents met the inclusion criteria and 42 of them

were convenience sampled and included for participation. After the test session (conducted 3

to 32.9 weeks; mean 17.7 weeks, prior to the experimental session) 3 participants withdrew from further participation. Two participants were using SSRIs and were excluded from further participation. Four participants vomited in response to the amino acid mixture and one participant refused to ingest the amino acid mixture, and their data were excluded from all statistical analyses. The remaining 32 participants completed the whole experiment and were included into all analyses.

ATD was achieved through a mixture of amino acids devoid of tryptophan as described previously (Zepf et al., 2008). The ingredients of the liquid mixtures in both conditions were consistent with the receipts used with children and adolescents in a previous study (Zepf et al., 2008). It was dosed according to bodyweight, and contained the following amount of amino acids per 10 kg: L-phenylalanine 1.32 g, L-leucine 1.32 g, L-iso-leucine 0.84 g, L-methionine 0.5 g, L-valine 0.69 g, L-threonine 0.6 g and L-lysine 0.96 g. During sham depletion, the mixture also contained L-tryptophan (0.70 g per 10 kg) (Zepf, Wöckel, Poustka, & Holtmann, 2009).

The amino acids were mixed with 200 ml cold water, 10 ml chocolate syrup and 3 drops of citric essence. Participants were offered protein-free sweets and juices to ease the ingestion of the mixture, and were encouraged to swallow it as fast as possible to avoid the unpalatable taste. Participants' guesses of whether they had been in the active or placebo condition were no better than chance, with 25.8% of the participants guessing they had been in the placebo condition.

Participants and their parents received written and oral information, telling the participants to take low protein food the day before participation, to abstain from any food containing proteins after 8:00 pm the day before participation, and to fast from the morning at the study day. The session started at about 8:00 a.m. Following the collection of baseline

blood samples, the participants completed a questionnaire on mood. The amino acid mixtures were then given to the participants. During a four and a half hour long waiting period, participants read, socialized or watched emotionally neutral movies, always together with an experimenter. They were told not to sleep or eat anything but water, protein-free juices and sweets provided by the experimenter.

To prevent a lack of Nicotine-adenine dinucleotide (NAD, a tryptophan-derived vitamin) because of depletion, B-tonin, a drink of B vitamins, was administered one hour after the ingestion of the amino acid mixture. Two hours after the ingestion of the amino acid mixture, participants were each offered an apple. A second blood sample was collected at about 4, 5 hours after ingesting the amino acid mixture. The participants then performed the behavioural measures of impulsivity and completed the questionnaire on mood a second time. Participants were tested individually in separate rooms and during the debriefing they were given a protein-rich meal.

Behavioural and Clinical Measures

Clinical measure in the screening session.

The Functional Assessment of Self-Mutilation (FASM). To measure NSSI we administered the FASM (Lloyd, Kelley, & Hope, 1997 as cited in Lloyd-Richardson et al., 2007), a self-report questionnaire of the methods, frequency and functions of NSSI. The FASM has been used in studies of community and psychiatric samples of adolescents, which have yielded support for its psychometric properties (Guertin et al., 2001; Lloyd-Richardson et al., 2007; Nock & Prinstein, 2004, 2005). For instance, the concurrent validity of the FASM is supported by its significant associations with measures of depression (Guertin et al., 2001; Nock & Prinstein, 2005), current suicide ideation (Lloyd-Richardson et al., 2007) past suicide

attempt (Guertin et al., 2001), recent suicide attempt and hopelessness (Nock & Prinstein, 2005). A Norwegian version of the FASM was used. The translation of the FASM into Norwegian was performed by Fikke in cooperation with a bilingual person, with English as native language.

Clinical measures in the test session.

The Beck Depression Inventory (BDI). Depressive symptoms were measured with the BDI (Beck, Steer, & Garbin, 1988), a 21 item self-report measure of affective, behavioural, cognitive, and somatic symptoms of depression. Estimates of internal consistency reliability have ranged from 0.79 to 0.91 in samples of both community and outpatient adolescents (Adewuya, Ola, & Aloba, 2007; Ambrosini, Metz, Bianchi, Rabinovich, & Undie, 1991; Larsson & Melin, 1990; Marcotte, Alain, & Gosselin, 1999; Teri, 1982), while test-retest reliability have ranged from 0.74 to 0.98 depending on the time intervals between testing (Ambrosini et al., 1991; Larsson & Melin, 1990). The BDI shows good convergent and discriminant validity in adolescent samples of psychiatric hospital inpatients and high school students (Barrera & Garrison-Jones, 1988).

The Beck Anxiety Inventory (BAI). Anxious symptoms were assessed with the BAI, a 21-item self-report measure of anxiety, specifically developed to reliably discriminate anxiety from depression (Beck, Epstein, Brown, & Steer, 1988). In both community and clinical samples of adolescents, estimates of internal consistency reliability have ranged from 0.88 to 0.94 (Jolly, Aruffo, Wherry, & Livingston, 1993; Osman et al., 2002). Among inpatient adolescents, BAI shows moderate to high convergent validity (Jolly et al., 1993). The BAI total score seems sensitive to levels of anxiety severity reported by clinical and non-clinical adolescents (Osman et al., 2002).

The State-Trait Anger Expression Inventory (STAXI). The experience of anger (both state and trait anger) and the expression of anger (anger directed inward and outward as well as attempts to control anger) were measured using the STAXI (Spielberger, 1988). It consists of 44 items that are rated on 4-point Likert scales, with higher scores indicating greater intensity or frequency of experienced or expressed anger. Adequate internal consistency and construct validity have been reported for the subscales of this inventory (Spielberger, 1988), which has been used with adolescents (Guertin et al., 2001; Lehnert, Overholser, & Spirito, 1994). A Norwegian adaptation of the STAXI, that is found to have quite similar psychometric properties and factor structure as those of the original American version (Håseth, 1996), was used.

Kiddie-Sads-Present and Lifetime Version (K-SADS-PL). To investigate the presence of psychiatric diagnoses, the K-SADS-PL (Kaufman et al., 1997) was administered by a clinical psychologist. It is a semi-structured diagnostic interview assessing current and lifetime history of psychopathology in children and adolescents according to criteria from the DSM-IV (American Psychiatric Association, 1994). The K-SADS-PL has demonstrated high inter-rater agreement (range: 93% to 100%), good to excellent test-retest reliability kappa coefficients (0.63-1.00), and its concurrent validity is supported, as evidenced by associations with self-report scales (Kaufman et al., 1997). The following diagnoses were considered particularly relevant and were examined: MDD, Generalized Anxiety, Obsessive Compulsive Disorder, Panic Disorder, Social Phobia, PTSD, Anorexia Nervosa, Bulimia Nervosa, Attention Deficit Hyperactivity Disorder (ADHD), Alcohol Abuse and Substance Abuse.

Neuropsychological measures in the test session.

Wechsler Abbreviated Scale of Intelligence (WASI). WASI (Psychological Corporation, 1999*)* provides a brief estimate of intelligence. It consists of four subtests:

Vocabulary, block design, similarities, and matrix reasoning. The WASI has excellent reliability and stability (Strauss, Sherman, & Spreen, 2006). Reliability coefficients are .96, .96 and .98 for the Verbal IQ (VIQ), Performance IQ (PIQ) and Full-Scale IQ (FSIQ), respectively (Strauss et al., 2006). The concurrent validity of the WASI is supported by findings showing a significant correlation (r=.89) between the WASI FSIQ score and the Kaufman Brief Intelligence Test Composite IQ score (Hays, Reas, & Shaw, 2002).

To measure each of the main aspects of executive functions, i. e., shifting, updating and inhibition (Miyake et al., 2000), we selected three tests from the Cambridge Neuropsychological Test Automated Battery (CANTAB; Cambridge Cognition, 2006). This is a widely used tool for assessing neuropsychological functions (Kyte et al., 2005) and the different CANTAB tasks are sensitive to neuropsychological impairments in a variety of populations (see Strauss et al., 2006, for a review). Tests from the CANTAB have been successfully employed in several adolescent populations (De Luca et al., 2003; Kyte et al., 2005; Matthews et al., 2008). The three tests were as follows:

The Intra/Extradimensional (IED) Set Shift . We administered the IED Set Shift (CANTAB; Cambridge Cognition, 2006) to measure the shifting aspect of executive functions. The subject must learn which of two presented stimuli is correct, assisted by feedback from the computer. Initially, two stimuli of one dimension (pink shapes) are shown, then each of two dimensions (pink shapes and white lines) are shown. The stimuli and/or rules change after six consecutive correct responses (the criterion of learning at each stage). These shifts are initially intradimensional (pink shapes are the relevant dimension), then extradimensional (white lines become the relevant dimension). The test terminates if at any stage the subject fails to reach the criterion of learning after 50 trials. The variables of interest were Stages completed, Pre-ED errors and EDS errors, reflecting the number of stages

34

completed successfully, the number of errors made prior to the extra-dimensional shift and in the extra-dimensional stage of the task, respectively.

Figure 2. The IED Set Shift Test
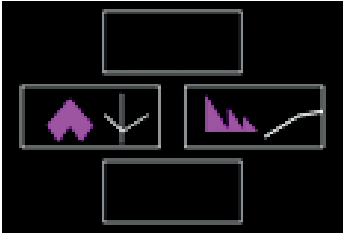
The Spatial Working Memory (SWM) Test. We measured the updating aspect of executive functions with the SWM test (CANTAB; Cambridge Cognition, 2006). Specifically, this test measures updating and monitoring of spatial information in working memory. The screen displays a number of boxes. The subject has to find one token in each box and use them to fill up a column on the side of the screen. Gradually, the number of boxes increases from three to eight. Touching any box where a token has already been found is an error. The subject decides the order in which boxes are visited. The variables of interest were Total errors and Strategy, reflecting the number of errors made and the use of an efficient strategy for completing the task, respectively.

Figure 3. The Spatial Working Memory Test
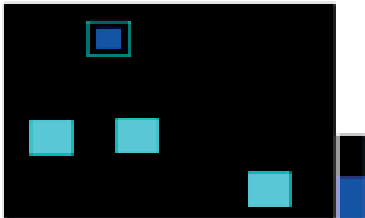
The Stop Signal Task (SST). The SST (Logan, Cowan, & Davis, 1984) is also part of the CANTAB (Cambridge Cognition, 2006) and was administered to measure the inhibition aspect of executive functions. Specifically, this test measures inhibition of dominant responses. The screen shows a white ring, in which a left-or right pointing arrow is displayed. First, the subject has to press the left button on a press pad when seeing a left-pointing arrow, and the right button when seeing a right-pointing arrow. In the second part of the task, the subject has to continue pressing the buttons as before, but has to withhold pressing the button if hearing a beep. The variables of interest were Direction errors on stop and go trials and Stop Signal Reaction Time (SSRT) last half, expressing the number of times the subject pressed the wrong button and the time between the stop signal and the inhibition of the response, respectively (Eagle et al., 2007; Logan & Cowan, 1984). A model accounts for response inhibition in the stop-signal paradigm in terms of a "horse race" between two sets of processes, one that generates a response for the primary task and one that responds to the stop signal (Logan & Cowan, 1984). If the primary-task process finishes before the stop-signal process, the response is executed, but if the stop-signal process finishes before the primary-task process, the response is inhibited (Logan & Cowan, 1984). Research findings (De Jong, Coles, Logan, & Gratton, 1990) support a major assumption underlying the horse race model, namely that the respective primary-task and stopping processes are independent (Logan & Cowan, 1984).

Figure 4. The Stop Signal Task
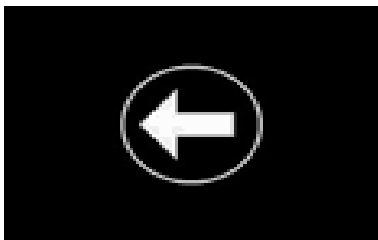
Children's Auditory Verbal Learning Test-2 (CAVLT-2). The CAVLT-2 (Psychological Assessment Resources, 1993) was administered to measure auditory verbal learning and memory. In the first free-recall word list, 16 words are presented to be remembered, followed by immediate recall. This is repeated for five trials. A sum score of correctly recalled words in trials 3, 4 and 5 comprises *level of learning*. In *the interference trial*, a second free-recall word list, the interference list, composed of 16 new words, is presented to the subject who immediately recalls as many words as possible from this list. *Immediate memory span* is computed by adding correctly recalled words in trial 1 of the first list and correctly recalled words in the interference list. Immediately following recall of the interference list, the individual is asked to recall words only from the first list, constituting *the immediate recall trial*. After 15 to 20 minutes the individual is again asked to recall words from the first list, representing *the delayed recall trial*. Lastly, the recognition list is read to the individual. All words from the first list, half of the words in the interference list and eight new words are included. Following the presentation of each word, the individual is asked to say "yes" if the word was in the first list and "no" if it was not, comprising *the recognition accuracy score*. *Total intrusions* are the sum score of incorrectly recalled words throughout all trials except the recognition trial. Three variables were computed to investigate loss of information between the learning phase and immediate and delayed recall and between immediate and delayed recall. The first was computed by subtracting the immediate recall score from the level of learning score, the second by subtracting the delayed recall score from the level of learning score, and the third by subtracting the delayed recall score from the immediate recall score. In a study with adolescents, findings have yielded support for the validity of the results from the CAVLT-2 (Talley, 1993). For instance, scores on the

immediate memory span was significantly correlated with reading and scores on the delayed recall was significantly correlated with mathematics, supporting the convergent validity of the results from the CAVLT-2 (Talley, 1993).

Behavioural measures in the experimental session.

The Continuous Performance Test, Identical Pairs Version (CPT-IP). We administered the CPT-IP (Cornblatt, Risch, Faris, Friedman, & Erlenmeyer-Kimling, 1988) to measure impulsive action. Four- digit numbers and nonsense shapes are visually presented in two trials. Each stimulus appears on the screen for 50 msec, presented at a constant rate of one per second. The subject's task is to respond as fast as possible whenever two identical stimuli are presented in a row. A correct identification of a matching set is called a "hit," while a response to a stimulus similar, but not identical to the preceding stimuli is called a "false alarm." Based on hits and false alarms, signal detection indices (e.g., β and d') are calculated. The β value is a measure of response style and captures subjects' tendency to over- or underrespond in situations with competition between behavioural suppression and active responding (Cornblatt et al., 1988; Walderhaug, Herman, Magnusson, Morgan, & Landrø, 2010). Lower β values, reflecting over- responding, indicate an impulsive response style (Conners, Epstein, Angold, & Klaric, 2003), and are related to ADHD symptoms (Epstein et al., 2003). Higher β values reflect a more cautious response style (Strauss et al., 2006) and are associated with depression (Johnson & Magaro, 1987). The d' is a measure of sensitivity or discriminability and involves the participant's sensory capability (Rutschmann, Cornblatt, & Erlenmeyer-Kimling, 1977) and attentional capacity (Cornblatt & Malhotra, 2001). The higher the score the better the performance (Rutschmann et al., 1977).

The Matching Familiar Figures Test (MFF20). To measure reflection impulsivity, we administered the MFF20 (Cairns & Cammock, 1978). This test consists of 20 test items.

Following the administration of two practice items, the subject is shown a picture of an object and six similar stimuli, of which only one is identical to the object (Kagan, Pearson, & Welch, 1966). The subject is asked to select the stimulus that is identical to the object (Kagan et al., 1966). The primary variables of interest were the mean latency to first response, the total number of errors committed, and the impulsivity or "I" score, which was calculated by subtracting the standard score of the mean latency to first response from the standard score of the total number of errors committed ($Z_e - Z_1$) (Salkind & Wright, 1977). The usefulness of the MFF20 with adolescents is supported by findings showing moderate stability for the latency, error and "I" scores respectively, as well as a high negative latency-error correlation (Messer & Brodzinsky, 1981).

The Profile of Mood States (POMS). To measure the effect of ATD on mood, we administered the POMS (McNair, Lorr, & Droppleman, 1971). It consists of 65 adjectives and the subject's task is to indicate how he/she feels at that moment by rating the degree to which his or her current mood state corresponds to the respective adjectives. The intensity of each mood adjective is rated from "not at all" to "extremely" on a 5-point Likert scale. Two total mood disturbance (TMD) scores were calculated by adding the sum scores for all the subscales of the POMS (i.e., tension-anxiety, depression-dejection, anger-hostility, vigor-activity, fatigue-inertia, and confusion-bewilderment; weighting vigor-activity negatively), at baseline and six hours after the ATD, respectively. To assess mood change, a mood change variable was calculated by subtracting the TMD score at baseline from the TMD score six hours after intake of the amino acids. The internal consistency reliability is .84 or greater for the six POMS scales (Spielberger, 1972). The validity of the POMS for the measurement of transitory mood states have been questioned (Spielberger, 1972). However, the POMS has repeatedly been used in studies investigating mood effects of ATD (see Mendelsohn, Riedel,

& Sambeth, 2009, for a review), and importantly has been able to capture mood effects of ATD (Walderhaug et al., 2007).

Assessment of Plasma Tryptohan Concentration in the Experimental Session

The analysis of total tryptophan was performed using a Biochrom 30 amino acid analyzer (Biochrom Ltd., England). This system uses ion exchange chromotagraphy with lithium buffers, post-column ninhydrin derivatization and photometric detection at wavelength 570 nm. Prior to analysis of total tryptophan, plasma samples were deproteinized by sulfosalicyclic acid. In the amino acids separation, a series of buffer solutions were run through a column using cation exhange resin, containing the amino acids in solution. The amino acids were then derivatizated, reacting with ninhydrin and detected at wavelength 570nm. An external standard (Sigma-Aldrich) was used for calibration.

Statistical Analyses

The Statistical Package for the Social Sciences (SPSS) for Windows (version 16.0 and 18.0; Inc., Chicago, IL, USA) was used to register and analyze all data. As reported in all three papers, one-way between-groups analyses of variance (ANOVAs) were completed to assess group differences in continuous demographic and psychometric variables. Group comparisons in frequencies of each diagnosis scored as 0 (not present) or 1 (present) were performed using chi-square tests. In instances of group differences in frequencies of diagnoses, one-way ANOVAs were conducted to explore the main effects of each of the given diagnoses (present versus not present) on the mean Z score of the variables on each executive function test (paper I) and on scores of each learning and memory variable (paper II). In instances of main effects of the given diagnoses on any of the neuropsychological variables, the given diagnoses were included as additional fixed factors in further analysis investigating

the effect of group (NSSI group(s) versus control group) only on the specific neuropsychological variables in which the preliminary analyses revealed main effects of the given diagnoses.

Paper I. Scores on the dependent variables on the three tests of executive functions were converted to Z scores. In doing so, we were able to make mean Z scores, reflecting the mean scores of the variables on each executive function test for each participant; one for the IED test variables, one for the SWM test variables and one for the SST variables. When positive scores on the dependent variables on the executive function tests had opposite meanings in their interpretation, some of them were reversed accordingly.

Two-way between-groups ANOVAs were performed to explore the main effects of group (control group, low severity NSSI group, high severity NSSI group) and sex and their possible interaction effects on the mean Z score of the variables on each executive function test. Only when these initial analyses yielded significant effects, further two-way ANOVAs with scores on each variable on the relevant executive function test as the dependent variables, were completed. When interaction effects between group and sex were found, post-hoc comparisons were performed using a dummy variable with six values representing the six possible combinations of group and sex (3*2). All post-hoc comparisons were performed using the Fisher's Least Significant Difference test.

Paper II. Two-way ANOVAs were completed to explore the main effects of group (NSSI versus control) and sex, and their interaction effects on scores of each learning and memory variable. When interaction effects between group and sex were found, post-hoc comparisons were performed using a dummy variable with four values representing the four combinations of group and sex (2*2). All post-hoc comparisons were applied using Bonferroni corrections.

Paper III. We employed one sample t-tests to assess the effects of ATD and sham depletion on plasma tryptophan concentrations. One-way ANOVAs were performed to assess the effects of group (active depletion versus sham depletion) on the impulsivity measures and on the mood change variable, respectively.

Ethical Considerations

The study was carried out in accordance with the Helsinki Declaration and approved by the Regional Committee for Medical Research Ethics (REK sør-øst) and the Norwegian Social Science Data Services (NSD). A researcher met all potential participants in their classrooms, informing them about the study. The adolescents also received written information, including one to their parents. Before participation, all participants and their parents signed informed consents. Still, the study raises some ethical issues.

First, without doubt the use of the self-report questionnaires and the diagnostic interview would reveal that some of the adolescents engaged in NSSI and/or had psychological problems. Indeed, this clinical assessment could reveal that some of the adolescents even met the criteria for one or several mental disorders. Thus, the research team developed a thorough plan to ensure that participants who revealed that they were struggling and were in need of help, would be followed up adequately. In brief, a network comprising the research team, the school health services, the local mental health services and two clinical psychologists, was established. Before we commenced the study, all the above mentioned were contacted and informed about the study. In the screening session, all participants were given oral and written information about the health service associated to their school, which they could contact if needed. Also, after the screening session all schools were contacted by the research team to get to know whether there had been any reactions of any kind among the participants in response to having completed the questionnaire on NSSI. Throughout all the

study sessions, the most suitable unit within the established network was contacted by the research team and hence made available for participants in need of professional help. In more serious cases, such as severe depression or social problems, needing a referral to the local mental health services, parents were informed. This was always in colloboration with the participants.

Second, the participants would not necessarily have a direct benefit from the results of any of the study sessions. Still, the results might come to the benefit of other adolescents at a later time. Also, in instances where professional help was needed, study results for the individual participant was provided if asked for.

Third, the experimental session involved the use of ATD. In brief, ATD presupposes fairly strict rules regarding food intake the day before the study followed by fasting on the actual study day. In addition, although no serious side effects have been reported, there have been a few cases of nausea, vomiting and diarrhoea in response to ATD (see Moore et al., 2000, for a review; Young, Smith, Pihl, & Ervin, 1985). Thus, exposing adolescent participants to ATD involving fasting and potential uncomfortable side effects, represent an ethical issue.

However, ATD is described as a safe method as its effects are rapidly reversed by consuming a normal diet (Bell, Hood, & Nutt, 2005). In accordance with this, all participants were served a high-protein meal immediately after having completed all the behavioural tests. Furthermore, ATD is a well-known method that has been used in several studies with healthy and various clinical samples (see Moore et al., 2000, for a review). A modified version of ATD in which the amount of amino acids to be ingested are dosed according to the participants' body weight, have been developed specifically for research with children and adolescents (Zepf et al., 2008). In a previous study using this modified version of ATD with

male children and adolescents with ADHD, no side effects were reported (Zepf et al., 2008). Nevertheless, as no previous studies had been conducted with female adolescents engaging in NSSI, an experimenter was always together with the participants in case of any unforeseeen reactions to the depletion. Importantly, ATD makes it possible to study the effects on impulsivity and mood of decreased serotonin neurotransmission in humans (Delgado et al., 1990). Such experimental studies are essential to gain further knowledge on causal relationships that might be involved in for instance NSSI. Thus, by using this method one might gain important, novel knowledge which can come to the benefit of other adolescents at a later time.

Results

Paper I

There were no significant group differences in sex ratios or on any IQ indicators. No significant group differences were found in frequencies of any diagnoses with the exception of current MDD [control group=0%, low-severity NSSI group=10.7%, high-severity NSSI group=21.2%, χ^2=8.19, df=2, p<.02] and previous MDD [control group=0%, low-severity NSSI group=0%, high-severity NSSI group=15.2%, χ^2=10.22, df=2, p<.01]. No main effects of either current or previous MDD on the mean Z scores of the IED variables, the SWM variables or the SST variables, respectively, were found. Thus, they were not included into further analyses.

No significant group or sex differences or any interaction effect between group and sex were found on the mean Z score of the IED variables.

On the mean Z score of the SWM variables, there were significant group differences [F(5, 91)=3.98, p=.02, η^2=.08]. There were no significant sex difference or interaction effect between group and sex. Post-hoc comparisons revealed no significant group differences. Significant group differences were found on the SWM Total error score [F(5, 91)=4.08, p=.02, η^2=.08] but no sex difference was found. There was a trend towards a significant interaction effect between group and sex [F(5, 91)=2.75, p=.07, η^2=.06]. A scatter plot inspection of these results revealed that the significant main effect of group was caused by the interaction effect of sex. Post-hoc comparisons showed that males in the high-severity NSSI group had a higher score than both males (p=.00) and females in the control group (p=.03). On the SWM Strategy score, there were significant group differences [F(5, 91)=3.52, p=.03, η^2=.07]; the high-severity NSSI group had a higher score than the low-severity NSSI group (p=.04). No significant sex difference or interaction effect between group and sex emerged.

On the mean Z score of the SST variables, there were significant group differences [$F(5, 91)=6.26$, $p=.00$, $\eta^2=.12$]; the low-severity NSSI group had higher scores than the control ($p=.02$) and the high-severity NSSI group ($p=.01$), respectively. A trend towards a sex difference [$F(5, 91)=3.91$, $p=.05$, $\eta^2=.04$] was found, while no interaction effect between group and sex emerged. On the score on SST Direction errors on stop and go trials, there were significant group differences [$F(5, 91)=4.61$, $p=.01$, $\eta^2=.09$]; the low-severity NSSI group had a higher score than the control group ($p=.03$). There were no sex difference or interaction effect between group and sex. There were significant group differences on the score on the SSRT variable [$F(5, 91)=6.21$, $p=.00$, $\eta^2=.12$]; the low-severity NSSI group had a higher score than the high-severity NSSI group ($p=.00$). A trend towards a sex difference emerged [$F(5, 91)=3.71$, $p=.06$, $\eta^2=.04$], while no interaction effect between group and sex was found.

Paper II

There were no significant group differences in sex ratios or on the IQ score. No significant group differences were found in frequencies of any diagnoses except for current MDD [control group=0%, NSSI group=16.4%, $\chi^2=6.58$, df=1, p=.01]. There were no effects of current MDD on any of the learning and memory scores without on the level of learning score [$F(1,95)=4.74$, $p=.03$, $\eta^2=.05$]; those meeting the criteria for current MDD had lower scores than those without current MDD. Thus, current MDD was included into further analysis on the level of learning score only.

On the level of learning score, there was a significant group difference [$F(3,94)=9.06$, $p=.00$, $\eta^2=.09$]; the NSSI group had a lower score than the control group. No sex difference or interaction effect between group and sex was found. Current MDD was included as an additional independent variable into the analysis of the effect of group on the level of learning

score. The effect of current MDD disappeared, while there still was a trend towards a significant effect of group on level of learning [$F(2,94)=3.76$, $p=.06$, $\eta^2=.04$].

On the interference trial, no significant group difference or interaction effect between group and sex were found. There was a significant sex difference [$F(3,94)=5.53$, $p=.02$, $\eta^2=.06$]; the males had a lower score than the females.

On the immediate memory span score, there was a significant group difference [$F(3,94)=4.92$, $p=.03$, $\eta^2=.05$]; the NSSI group had a lower score than the control group. No significant sex difference or interaction effect between group and sex was found.

There were significant group differences on the immediate recall trial [$F(3,94)=6.87$, $p=.01$, $\eta^2=.07$]; the NSSI group had a lower score than the control group. No sex difference was found, while there was a significant interaction effect between group and sex [$F(3,94)=10.53$, $p=.00$ $\eta^2=.10$]. Post-hoc comparisons showed that males in the NSSI group had a lower score than males in the control group ($p=.01$). A scatter plot inspection of these results revealed that the significant main effect of group was caused by the inferior performance of the males in the NSSI group. On the delayed recall trial, there were significant group differences [$F(3,94)=5.20$, $p=.03$, $\eta^2=.05$]; the NSSI group had a lower score than the control group. There was no sex difference, while there was a significant interaction effect between group and sex [$F(3,94)=5.95$, $p=.02$ $\eta^2=.06$]. Post-hoc comparisons revealed that males in the NSSI group had a lower score than males in the control group ($p=.04$). A scatter plot inspection of these results revealed that the significant main effect of group was caused by the inferior performance of the males in the NSSI group. On the recognition accuracy score, no significant sex or group difference was found, while there was a significant interaction effect between group and sex [$F(3,94)=5.74$, $p=.02$, $\eta^2=.06$]. Post-hoc comparisons revealed that males in the NSSI group scored lower than females in the NSSI group ($p=.01$).

No significant group or sex differences or any interaction effect between group and sex were found on the total intrusions score, the scores reflecting loss of information between the learning phase and immediate and delayed recall, respectively, or between immediate and delayed recall.

Paper III

As expected, ATD significantly decreased plasma concentrations of total tryptophan ($t(16) = -19.2$, $p<.000$). Following ATD, the average decrease in total tryptophan level, was 78.9%. Sham depletion significantly increased plasma concentrations of total tryptophan ($t(14) = 7.8$, $p<.000$). The average increase in total tryptophan level was 276.6% following sham depletion.

There were no significant differences between the respective active depletion and sham depletion groups in age, on any of the IQ scores or in frequencies of any of the psychiatric diagnoses.

In the number mode of the CPT-IP, ATD had a statistically significant effect on the β score ($F(1, 30)=8.73$, $p=.01$); the active group had a lower β score as compared with the placebo group. Furthermore, ATD had a statistically significant effect on the d' score ($F(1, 30)=5.66$, $p=.02$); the active group had a higher d' score than the placebo group. ATD had a statistically significant effect on the hit score ($F(1,30)=5.37$, $p=.03$); the active group had a higher hit score than the placebo group. However, no ATD effect was found on the false alarm score. In the shapes mode of the CPT-IP, ATD had no statistically significant effects on the β, d', hits or false alarms scores, respectively.

ATD had no statistically significant effects on any of the scores on the three MFFT variables, ie. on the mean latency to first response, on the total number of errors committed, or on the "I" score. Also, ATD had no effect on the mood change score.

Summary of Papers

Paper I

Background. The aim of this study was to investigate three main aspects of executive functions (EFs), i.e. shifting, updating and inhibition, in adolescents engaging in non-suicidal self-injury (NSSI) as compared with healthy controls. **Method.** EFs were assessed using the Intra/Extradimensional Set Shift, the Spatial Working Memory (SWM) Test and the Stop Signal Test (SST) from the Cambridge Neuropsychological Test Automated Battery (CANTAB), in a high-severity NSSI group (n=33), a low-severity NSSI group (n=29) and a healthy control group (n=35). Diagnostic characteristics were examined using the Kiddie-Sads-Present and Lifetime Version. **Results.** There were group differences on the SWM Test. A trend towards an interaction effect of sex revealed that males in the high-severity NSSI group made significantly more errors than males and females in the control group.

Both males and females in the high-severity NSSI group made poor use of an efficient strategy in completing the test. The low-severity NSSI group performed poorly on the SST, making more errors than the control group and showing an impaired ability to inhibit initiated responses, as compared with the high-severity NSSI group. There were group differences in frequencies of current and previous major depressive disorder. However, no effects of these diagnoses were found on any of the EF tests. **Conclusions.** This study demonstrates that NSSI subgroups have distinct deficits in EFs. The high-severity NSSI group has working memory deficits, while the low-severity NSSI group has impaired inhibitory control. This supports the emotion regulation hypothesis.

Paper II

Background. To obtain further knowledge on the neuropsychological correlates of non-suicidal self-injury (NSSI), various aspects of verbal learning and memory were

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investigated in adolescents engaging in NSSI as compared with healthy controls. **Method.**
Verbal learning and memory was assessed using the Children's Auditory Verbal Learning
Test-2 in a NSSI group (*n*=62) and a healthy control group (*n*=36). **Results.** The NSSI group
performed below the control group on measures of immediate memory span and level of
learning. Although males in the NSSI group had impaired recall and recognition, they
remembered most of what they learned. No group differences were found on the intrusion or
the interference measure. **Conclusions.** Adolescents engaging in NSSI exhibit impairments in
verbal learning and memory. The core problems involve impaired short-term
memory/working memory and difficulty in the encoding of material into long-term memory.
This suggests that an inefficient network comprising frontal cortex and more posterior
structures are involved in NSSI. Furthermore, the findings might be seen as a first reasonable
step in investigating whether adolescents engaging in NSSI may need training to improve
their verbal learning and memory, which in turn might affect their academic attainments.

Paper III

Background. Non-suicidal self-injury (NSSI) has repeatedly been associated with
impaired emotion regulation and impulsivity. Low serotonin (5-HT) function is associated
with NSSI, impaired emotion regulation and impulsivity. We investigated the effects of
experimentally lowered 5-HT activity, via acute tryptophan depletion (ATD), on impulsive
action, reflection impulsivity and mood in female adolescents engaging in NSSI. **Method.**
Thirty-two female adolescents engaging in NSSI participated in a randomized, double-blind,
parallel group ATD study. Following ATD, impulsive action was assessed using the
Continuous Performance Test, Identical Pairs Version and reflection impulsivity was assessed
using the Matching Familiar Figures Test. Mood-lowering was examined using the Profile of
Mood States. **Results.** Following ATD, the participants adopted an impulsive response style.

ATD did not affect reflection impulsivity or mood. **Conclusions.** In addition to causing an impulsive response style, ATD caused increased attentional capacity. Thus, the impulsive response style was characterized as being focused and directed, as one of functional impulsivity resulting in an optimal test performance. The findings might suggest that low serotonin function triggers this particular group of female adolescents to impulsively engage in NSSI when in emotional distress.

Discussion

The overall aim of the present study was to gain more knowledge on some potentially relevant factors concerning the reasons why adolescents engage in NSSI. Within this wide, far-reaching context, we investigated various aspects of neuropsychological functions in adolescents engaging in NSSI, as well as the effects of low serotonin function, via acute tryptophan depletion, on impulsivity and mood in female adolescents engaging in NSSI. The study was well-designed to address the specific research aims. Still, a critical examination and discussion of the findings are needed to yield some indications as to what the findings actually might mean. In addition, some methodological issues need to be addressed. Nevertheless, the present findings might help illuminate some aspects of the neuropsychological and serotonergic functioning that might be involved in NSSI. Thus, in essence the present research findings contribute to the puzzle of understanding why adolescents engage in NSSI.

Discussion of Main Findings

As reported in paper I, with respect to the investigation of the three main aspects of executive functions, i.e., shifting, updating and inhibition (Miyake et al., 2000), we found that the high-severity NSSI group had working memory deficits, while the low-severity NSSI group had impaired inhibitory control. Neither NSSI subgroups had shifting deficits. No significant group differences in IQ strengthen the conclusion that the results reflect impairments in specific aspects of executive functions and not group differences in general cognitive abilities. Furthermore, those meeting criteria for a current or a previous MDD did not perform worse on the executive function tests than those who did not meet the criteria. This indicates that the impairments in executive functions in adolescents engaging in NSSI is not just an expression of an underlying psychological disorder. The working memory deficits

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were most pronounced in males in the high-severity NSSI group, however, the same pattern was evident in their female counterparts.

These findings suggest that the NSSI subgroups have selective deficits in executive functions, thereby yielding knowledge regarding specific aspects of neuropsychological functioning that might be involved in NSSI in adolescents. Both working memory and inhibition are related to emotion regulation (Nash et al., 2007; Schmeichel et al., 2008; Van Dillen & Koole, 2007). Consequently, the findings of selective deficits in these aspects of executive functions might suggest that the ability to regulate emotions *per se* is impaired in adolescents engaging in NSSI, thereby indirectly suggesting that they struggle with regulating their emotions. Along these lines, the present neuropsychological findings corroborate and extend previous findings showing that adolescents typically report that they engage in NSSI to regulate their emotions (Kumar et al., 2004; Laye-Gindhu & Schonert-Reichl, 2005; Nock & Prinstein, 2004; Penn et al., 2003; Ross & Heath, 2003). In sum, the present findings might indirectly support the emotion regulation hypothesis of NSSI from a neuropsychological perspective.

As reported in paper II, the systematic investigation of the various subcomponents of verbal learning and memory revealed that adolescents engaging in NSSI had impaired immediate memory span and verbal learning. In addition, males in the NSSI group had deficits in immediate and delayed recall and in recognition. However, they remembered most of what they learned, suggesting that their primary difficulties reside in a reduced amount of learning or encoded information to begin with, rather than additional impairments in recall and recognition as such. No group differences were found on the intrusion or the interference measure. Again, no group differences in IQ strengthen the conclusion that the results reflect

deficits in specific aspects of verbal learning and memory and not between-group differences in intellectual functioning.

The finding of impaired immediate memory span extends the findings reported in paper I of impaired spatial working memory in adolescents engaging in NSSI, suggesting impaired short-term memory and working memory irrespective of modality in this specific group of adolescents. Importantly, tasks that primarily are short-term memory tasks for some individuals are working memory tasks for others because individuals differ in reliance on the central executive in performing the tasks (Engle, Tuholski, Laughlin, & Conway, 1999). Furthermore, the finding of impaired verbal learning suggests difficulty in long-term memory encoding abilities (Talley, 1993). However, MDD also had a significant effect on the particular measure reflecting long-term memory encoding abilities. Still, the effect of NSSI on this measure remained nearly significant, whereas the effect of current MDD disappeared, when included in the same analysis. Thus, although only at trend-level, NSSI continued to have an effect on verbal learning when controlling for MDD.

Besides the results regarding long-term memory encoding abilities, the findings suggest that deficits in specific aspects of verbal learning and memory are associated with NSSI independently of psychiatric diagnoses. Importantly, the findings might be relevant in applied settings as scores on verbal learning and memory tests are associated with academic achievements (Talley, 1993). As we did not include a measure of academic attainments, we cannot know whether performance on verbal learning and memory tests predict scholastic achievements in this particular adolescent group. Nevertheless, the present findings might be seen as a first reasonable step in investigating whether adolescents engaging in NSSI may need training to improve their verbal learning and memory, which in turn might affect their academic attainments.

In addition, the findings contribute further to the comprehension of some aspects of neuropsychological functioning that might be involved in NSSI. Impaired short-term memory/working memory might be one underlying problem in adolescents engaging in NSSI, as these impairments might indirectly contribute to their difficulty in regulating emotions, as discussed above. Furthermore, the struggling with regulating emotions in these adolescents might in turn consume their cognitive resources that are necessary for verbal encoding of memories, thereby possibly in a viscous circle, further aggravating their impaired learning and short-term memory/working memory (Richards & Gross, 2000). At a neurobiological level, this constellation of findings suggests an inefficient network comprising frontal cortex structures and more posterior cortical structures being involved in NSSI.

As reported in paper III, the main finding in the experimental session of the study was that ATD caused increased impulsive action in female adolescents engaging in NSSI. However, ATD did not affect reflection impulsivity or mood in the female adolescents. Unexpectedly, ATD also caused increased discriminability and attention. Thus, their impulsive response style following ATD appeared focused and directed. This contrasts with the prevailing conceptualization of impulsive behaviours, as engaged in impetuously, lacking deliberation and regard for the consequences (Cherkasky & Hollander, 1997). In sum, as the response style adopted by the tryptophan-depleted female adolescents resulted in an optimal test performance, it can perhaps be best described as one of functional impulsivity (Dickman, 1990). Intriguingly, our findings corroborate previous findings of this specific type of impulsive response style following ATD with remitted depressed patients with a history of suicidal ideation (Booij et al., 2006), suggesting that low 5-HT function leads to a specific type of focused and directed impulsive response style in these quite similar groups struggling with self-injury. Furthermore, ATD had no effects on reflection impulsivity in female

adolescents engaging in NSSI, suggesting that low 5-HT function and impulsive action are specifically involved in NSSI. The findings of increased impulsive action and no mood-lowering following ATD might suggest that female adolescents engaging in NSSI have a reflexive tendency toward impulsive action, as opposed to a reflexive tendency toward freezing, avoidance and inaction, associated with depression vulnerability (Carver, Johnson, & Joormann, 2008). In sum, the ATD findings might suggest that low serotonin is involved in impulsive action in this adolescent group, and further that this specific type of impulsive action might be triggered in the face of psychological distress. Specifically, the findings might imply that low serotonin function triggers this particular group of female adolescents to impulsively engage in NSSI when in emotional distress. As adolescents typically report that their negative emotions are reduced during and after self-injuring (Laye-Gindhu & Schonert-Reichl, 2005; Ross & Heath, 2003), the present finding of impulsive action following ATD might possibly be relevant for emotion regulation in female adolescents engaging in NSSI.

Summing up, the main findings of the study advance the understanding of specific aspects of neuropsychological functioning that might be involved in NSSI in adolescents. Impaired executive functions seem to be particularly involved in NSSI. Also, the findings contribute to elucidate the role of low serotonin function and impaired impulse control that might be involved in NSSI. However, some of the findings are in need of even further examination and discussion.

Findings with respect to impulsivity across NSSI subgroups and sessions. The Stop Signal Task (SST; Logan et al., 1984) and the Continuous Performance Test, Identical Pairs Version (CPT-IP; Cornblatt et al., 1988) used in the respective test and experimental sessions of the study, both measure impulsive action or the ability to inhibit a dominant motor response (Robbins & Crockett, 2010). As reported and discussed in paper I, only the low-

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severity NSSI group showed inhibition deficits, as measured by the SST. Thus, the high-severity NSSI group did not show impaired performance on the SST. However, when tryptophan-depleted (paper III), the adolescent females engaging in NSSI adopted an impulsive response style, as shown by their low β-value on the CPT-IP. An equal number of adolescent females in the low-and high-severity NSSI subgroups participated in the ATD session. Hence, although only one NSSI subgroup showed impulsivity in the ordinary neuropsychological test session (paper I), ATD triggered impulsivity in general in female adolescents engaging in NSSI (paper III).

Although the CPT-IP and the SST both measure the response inhibition aspect of impulsivity (Robbins & Crockett, 2010), there might be subtle differences in which aspects of response inhibition they measure (Robbins & Crockett, 2010). Presuming that the CPT-IP requires Go/NoGo discrimination, in the CPT-IP, inhibition has to be exerted in the response selection phase (Robbins & Crockett, 2010). On the contrary, in the SST, response selection has already occurred but the performance of the response has to be curtailed (Robbins & Crockett, 2010). Thus, our findings might suggest that the adolescents in the low-severity NSSI group struggle with behavioural disinhibition both *before* (CPT-IP) as well as *after* response selection (SST). Along these lines, our findings might further suggest that the impaired impulse control in the adolescents in the high-severity NSSI group only involves behavioural disinhibition *before* (but not *after*) response selection. Thus, the use of different tests measuring subtly different aspects of response inhibition might have captured distinct deficits in response inhibition in the two NSSI subgroups. However, in addition to the use of different response inhibition tests, the sessions of the study in which they were performed in, involved completely different conditions. We did not employ identical tests of response inhibition in the two sessions of the study. Accordingly, we can not disentangle whether the

inconsistent findings with respect to response inhibition in the high-severity NSSI group across study sessions, were due to the use of different tests or the different conditions in which they were performed. To be able to disentangle these different possibilities, we should have used exactly the same test of response inhibition in both sessions of the study.

Indeed, as described in paper I and paper III, the contexts in which the tests of response inhibition were completed, were to a high degree dissimilar. When completing the SST (paper I), the adolescents met at the Department of Psychology for undergoing a straightforward neuropsychological testing session. This represented a more or less neutral test situation, at least in the sense that we did not experimentally induce stress as the context for the testing session. In contrast, when completing the CPT-IP (paper III), the adolescents were exposed to ATD. Decreased serotonin neurotransmission, induced by ATD, might be understood as stress, even though it contrasts with the traditional focus on environmental stress. A main advantage of this biological operationalization of stress, is that the serotonin system is challenged directly, thereby eliminating individual differences in subjective perception and reporting of stress. As stress is experimentally induced, it is more controlled than naturally occurring negative life events, used as operationalizations of stress in previous studies (Dykman & Johll, 1998; Hankin, Abramson, Miller, & Haeffel, 2004). Adolescents engaging in NSSI typically report strong negative emotional states as leading up to self-injuring (Laye-Gindhu & Schonert-Reichl, 2005; Ross & Heath, 2003), suggesting that they might impulsively engage in NSSI only when under extreme stress or in psychological distress (Janis & Nock, 2009). Thus, the stressful context in which the CPT-IP was completed, might be analogous to the emotional distress that often is reported as leading up to self-injuring.

Hence, the findings reported in paper I and paper III might suggest that stress is needed to elicit an impulsive response style in adolescents in the high-severity NSSI group. This comprehension is compatible with two-mode models of self-regulation (Carver et al., 2008). Specifically, serotonin function is important for executive control processes that inhibit behaviour patterns influenced by the reflexive or reactive system (Carver et al., 2008). By temporarily decreasing 5-HT neurotransmission by ATD, the finding of increased impulsive action (paper III) suggests that female adolescents engaging in NSSI have a reflexive tendency toward impulsive action (Carver et al., 2008). Importantly, the reflexive system dominates when a situation is emotionally charged (Carver et al., 2008). Thus, stress either conceptualized as emotional distress or as experimentally induced lowered serotonin function, seems necessary to elicit or trigger an impulsive response style in adolescents in the high-severity NSSI group. This possibility is supported by no findings of increased impulsivity in this particular NSSI group in the ordinary test session as reported in paper I. Also, the impulsive response style elicited by ATD was focused and directed. Thus, it could perhaps be best described as one of functional impulsivity, as it resulted in a beneficial test performance on the CPT-IP. This specific directed impulsive response style elicited by ATD might be analogous to the impulsive response stye elicited in the face of emotional distress in real life in female adolescents engaging in NSSI. Accordingly, the functional impulsive response style found on the CPT-IP might indicate that this specific type of impulsive response style might be adaptive in regulating overwhelming emotions in the short run in these adolescents. Indeed, adolescents find engaging in NSSI as effective at releasing negative affect (Jacobsen & Gould, 2007). Nevertheless, engaging in NSSI likely have devastating effects in the long run, worsening symptoms and distress (Jacobsen & Gould, 2007) and precluding engaging in more abstract and verbal emotion regulation strategies (Ross et al., 2009). Interpreting the inconsistent findings on impulsivity in the high-severity NSSI group, as suggesting that stress

is necessary to trigger a specific impulsive response style in this particular adolescent group, is in accordance with vulnerability-stress models, stating that both a vulnerability and stress are needed for a mental disorder to develop (Monroe & Simons, 1991). Thus, the apparently inconsistent findings in the high-severity NSSI group discussed in paper I and paper III can be reconciled within such an understanding.

ATD triggered impulsivity in general in adolescents engaging in NSSI. However, stress was not necessary to elicit impaired response inhibition in the adolescents in the low-severity NSSI group (paper I). The findings of impaired response inhibition regardless of stress in the low-severity NSSI group might suggest that these adolescents differ in some respects from the adolescents in the high-severity NSSI group. There are individual differences in the degree to which adolescents engage in emotion-based rash action and risky behaviour (Cyders & Smith, 2008). The impaired response inhibition regardless of stress found in the adolescents in the low-severity NSSI group might suggest that they are on the one extreme on this disposition. Within such an understanding, their self-injuring might primarily reflect impulsive experimenting with these behaviours, rather than impulsively engaged in when in psychological distress primarily for affect-regulating purposes, which might seem to be the case for the high–severity NSSI group. Thus, reflecting their inclination towards engaging in impulsive, risky behaviours, the NSSI behaviours engaged in by the low-severity NSSI group might primarily reflect benign, clinically insignificant experimenting with these behaviours. This in contrast to the self-injuring nature of the same behaviours, reflecting pathological, clinically significant NSSI among the adolescents in the high-severity NSSI group.

The use of different NSSI subgroups. The investigation of executive functions in adolescents engaging in NSSI (paper I) was based on a neurobiological model of emotion

processing, recognizing the role of executive functions in regulating emotions (Phillips et al., 2003). In turn, our understanding of executive functions was based on the empirically supported model of executive functions as consisting of three main aspects, i.e., inhibition, updating and shifting (Miyake et al., 2000). The exploration of these aspects of executive functions in the adolescents engaging in NSSI was primarily theoretically driven. Specifically, it was aimed at increasing the knowledge of specific aspects of executive functioning that could further help illuminate why adolescents typically report that they engage in NSSI to regulate emotions (Kumar et al., 2004; Laye-Gindhu & Schonert-Reichl, 2005; Nock & Prinstein, 2004; Penn et al., 2003; Ross & Heath, 2003). However, NSSI is a heterogeneous phenomeneon (Lloyd-Richardson et al., 2007; Skegg, 2005; Whitlock et al., 2008). Thus, from a theoretical stance, it could be that different subgroups of adolescents engaging in NSSI have distinct deficits in different aspects of executive functions. Thus, to capture such possible differences between NSSI subgroups, we took the NSSI heterogeneity into consideration in our theoretically driven investigation of executive functions. Specifically, we classified the adolescents engaging in NSSI into a low- and a high-severity NSSI subgroup, respectively, when investigating executive functions in adolescents engaging in NSSI (paper I).

In contrast to the primarily theoretical stance from which the investigation of exeutive functions was performed (paper I), the investigation of the various aspects of verbal learning and memory (paper II), was at least initially driven by a more applied perspective. In essence, the typical age of onset of NSSI is between 12 and 14 years (Muehlenkamp & Gutierrez, 2007; Nock & Prinstein, 2004; Ross & Heath, 2002). This coincides with adolescence, an important period for the development of long-term patterns of academic functioning (Lerner, Ostrom, & Freel, 1997). In children and adolescents, previous studies have shown that various

aspects of verbal learning and memory are associated with academic attainments (Kinsella et al., 1995, 1997; Sujansky, Griffith, & Lefevre, 1996; Talley, 1993). Accordingly, one of the main aims of the investigation of verbal learning and memory in adolescents engaging in NSSI was to gain knowledge that could be relevant in applied settings. Specifically, the investigation could help illuminate whether adolescents engaging in NSSI need training to improve their verbal learning and memory, which might affect their academic attainments. Within this applied perspective, we aimed at investigating the level of functioning on verbal learning and memory *as such* in adolescents engaging in NSSI, independently of the severity of their NSSI. Thus, when investigating the various aspects of verbal learning and memory (paper II), we did not classify the adolescents engaging in NSSI into further subgroups reflecting low versus high NSSI severity. Instead we treated all adolescents engaging in NSSI as one NSSI group.

In the experimental session of the study (paper III), we primarily aimed at gaining knowledge about potential mechanisms as regards to serotonin function, impulsivity and mood that might be involved in NSSI. To achieve this goal, 42 of 48 of our overall sample of female adolescents engaging in NSSI, was convenience sampled to participate in the experiment. We decided not to include all female adolescents engaging in NSSI into the experiment for several reasons. First, based on previous ATD-studies (Menkes, Coates, & Fawcett, 1994; Weltzin, Fernstrom, McConaha, & Kaye, 1994) group sizes of approximately 15 adolescents would enable us to detect behavioural and mood effects of ATD. Thus, it was not necessary to include all the female adolescents in the experiment to investigate our research aims. Second, there are some potential uncomfortable aspects inherent in participating in an ATD-study, such as having to fast and ingest an unpalatable amino acid mixture. Hence, from an ethical perspective, it could hardly be justified to let more adolescents than strictly necessary to investigate our research aims, undergo the ATD-

procedure. In addition, for practical reasons, we decided to use a convenience sample of the female adolescents engaging in NSSI for participation in the experiment.

The influence of sex on the neuropsychological findings in adolescents engaging in NSSI. Some previous studies have found significant sex differences in executive functions (Anderson et al., 2001; Fields et al., 2009; Kalkut et al., 2009) and in verbal learning and memory (Kramer, Delis, Kaplan, O'Donnell, & Prifitera, 1997) in adolescents. Accordingly, we decided to investigate the interactive effect of sex when investigating these neuropsychological functions in adolescents engaging in NSSI. Overall, we found the same pattern of deficits in specific aspects of the investigated neurospychological functions in male and female adolescents engaging in NSSI. However, the results revealed some interactions between group and sex. Specifically, although the adolescents in the high-severity NSSI group in general showed impaired spatial working memory, the males in this group was somewhat particularly impaired in this respect. Also, the findings of deficits on measures of immediate memory span and level of learning, suggested a core problem involving impaired short-term memory/working memory and difficulty in the encoding of material into long-term memory in adolescents engaging in NSSI in general. However, as the females engaging in NSSI showed intact recall and recognition, they seemed to being able to compensate for these deficits. On the other hand, the males engaging in NSSI were not able to compensate for these deficits, as they also showed impaired recall and recognition.

Our findings revealing the presence of some interaction effects between different adolescent groups and sex in neuropsychological functions emphasize the importance of considering the interactive effect of sex when investigating neuropsychological functions in various groups in general and perhaps in adolescent groups in particular. Indeed, some research findings show different developmental trajectories for some neuropsychological functions in male and female adolescents (Kalkut et al., 2009). By investigating the

interactive effect of sex when possible, one might prevent overlooking sex differences that are specific for some groups. Importantly, such sex differences might be of relevance both with respect to the understanding of the phenomena of interest as well as to the development of adequate clinical interventions.

Methodological Considerations

Reliability of findings. The adolescents engaging in NSSI in the present study are probably not representative of the population of adolescents engaging in NSSI in the community of Oslo and nearby areas. The same issue of representativity applies to the healthy adolescent controls. Our sample, both with respect to the adolescents engaging in NSSI and the healthy control adolescents were not selected randomly from the respective populations of adolescents engaging in NSSI and adolescents who have never engaged in any NSSI. Instead, they chose to participate in response to a request, possibly reflecting a particular interest in participating in a study focusing on neuropsychological functioning. In addition, all adolescents participating in the present study attended school. Importantly, research findings show that children and adolescents who do not attend school have higher rates of psychopathology as compared with children and adolescents without attendance problems (Egger, Costello, & Angold, 2003). Thus, it is possible that our participants had a higher level of functioning and education as compared to the average community populations of adolescents who engage in NSSI and of adolescents who have never engaged in any NSSI, resepectively. This potential bias might have influenced the present research findings.

Also, the female adolescents engaging in NSSI that underwent the experimental session of the study, were convenience sampled from our pool of female adolescents engaging in NSSI. Again, this raises the question of the representativity of this sample of female adolescent group, and in turn the reliability of the findings from the experimental session. The

female adolescents were not randomly selected from either the population of female adolescents engaging in NSSI nor from the sample of female adolescents engaging in NSSI who participated in the present study. Again, this potential bias might have influenced the present research findings.

Furthermore, the relatively few males in our sample raise the question of the reliability of our findings with respect to deficits in specific aspects of executive functions and in specific aspects of verbal learning and memory in male adolescents engaging in NSSI. By interpreting our findings as reflecting real group differences, there is a risk of committing a type I error. However, rejecting our findings entails the possibility of committing a type II error. The risk of committing a type I error seems justified considering the potential negative consequences of ignoring our findings of specific neuropsycological impairments in male adolescents engaging in NSSI. However, the reliability of our findings with male adolescents engaging in NSSI will be strengthened if replicated with samples including more males.

External validity of findings. The participants in the present study were recruited exclusively from high schools. Thus, all participants, including the adolescents engaging in NSSI, were community sampled. Throughout all sessions of the study, the vast majority of the adolescents engaging in NSSI attended school and appeared to be functioning adequately. Thus, our community sample might differ from samples recruited exclusively from clinics, outpatient or inpatient units which often indicate a significant loss of functioning across a wide range of areas in their lives. Hence, one cannot know whether the present findings regarding adolescents engaging in NSSI can be generalized to clinical populations of adolescents struggling with NSSI.

However, as reported in paper I, the present findings show that the community sampled adolescents engaging in NSSI had elevated levels of symptoms of depression and

anxiety as well as of experienced and expressed anger. A considerable number of them met criteria for at least one psychiatric diagnosis, especially MDD. Although not identical and surely not of the same degree of severity, the present pattern of associated psychiatric symptoms and diagnoses in the adolescents engaging in NSSI resemble what is found in clinical samples of adolescents engaging in NSSI (Jacobsen et al., 2008; Nock et al., 2006). In addition, a substantial number of the community sampled adolescents engaging in NSSI had received or still received help from the school health services or the local mental health services. In sum, in certain respects the adolescents performing NSSI in the present study resembled clinical populations of adolescents engaging in NSSI. Nevertheless, as they were recruited exclusively from schools, they might differ from clinical populations of adolescents engaging in NSSI, in important ways that might have influenced the present findings.

Also, closely related, one might question whether the NSSI engaged in by the community sampled adolescents is the same phenomena of NSSI engaged in by clinical populations of adolescents. Indeed, the behaviours that qualify for NSSI and those that are of clinical significance are unresolved issues (Lloyd-Richardson et al., 2007). Still, as the questionnaire that we used to screen for NSSI has been used to capture NSSI in clinical samples of adolescents (Guertin et al., 2001; Nock & Prinstein, 2004), the NSSI phenomena, at least at a behavioural or phenomenological level, seems similar across samples. In addition, our decision to use as criteria for inclusion in the NSSI group that the adolescents had engaged in at least two different NSSI behaviours during the past year, was chosen to exclude adolescents only endorsing the item "picked at a wound," as it in isolation may reflect non-pathological, non–NSSI (Lloyd-Richardson et al., 2007). Furthermore, research findings show that the same biochemical dysfunction might underlie self-injurious behaviours that vary in

severity and aggression (Stanley et al., 1992), suggesting that the present findings might be generalizable to NSSI of varying severity.

Still, it seems reasonable to assume that the NSSI engaged in by the community adolescents in the present study might not be as severe as the NSSI engaged in by clinical populations of adolescents. Accordingly, the use of a community sample might seem to involve a particular conservative test when investigating specific aspects of neuropsychological functioning that might be involved in NSSI. Also, it seems reasonable to assume that the psychological problems reported by the community sampled adolescents engaging in NSSI, at least at a group level, were less severe as compared with psychological problems from which clinical adolescent populations suffer. Supporting this assumption, although a considerable number of the community sampled adolescents engaging in NSSI suffered from psychological problems, the vast majority of them attended school and appeared to function adequately in their lives throughout all sessions of the study. Thus, there are reasons to believe that the present findings with a community sample at least to a lesser extent are contaminated by impairments associated with clinical samples. This suggests that the present findings might give a clearer picture of the neuropsychological functions that might be involved in NSSI.

Nevertheless, studying such a community sample, which thus to a lesser extent is confounded by comorbid problems that might influence the results in a clinical sample, raises the question of the generalizability of the results to clinical populations. Ultimately, it is an empirical question whether the present findings are generalizable to adolescent clinical populations engaging in NSSI as well as to clinical populations engaging in NSSI at other age groups than adolescence.

Clinical Implications

The present findings involve statistically significant differences between groups on some behavioural measures of neuropsychological functioning. However, statistically significant group differences do not necessarily translate to clinically significant group differences. Thus, even though the findings show statistically significant differences between groups on specific aspects of neuropsychological functions, it remains an empirical question to find out whether the statistically significant group differences are of clinical relevance. This should be kept in mind when considering potential clinical implications of the present findings. Also, one has to be aware of the fact that the research findings are at a group level. Thus, one cannot know whether the findings and their ensuing clinical implications are relevant for each and every adolescent engaging in NSSI. However, the findings at the group level nevertheless show the importance of completing a neuropsychological and a clinical assessment when encountering the individual adolescent engaging in NSSI in a clinical setting. Indeed, the clinical implications primarily pertain to the neuropsychological and clinical assessment of adolescents engaging in NSSI.

First, as reflected in the findings, a neurospsychological assessment might yield important clinical information. Such an assessment might uncover selective deficits in specific aspects of executive functions as well as in aspects of verbal learning and memory that might be of clinical utility. Specifically, if such deficits are found in the individual adolescent struggling with NSSI, they should be taken in consideration when planning therapeutic interventions. Indeed, the present findings showing that NSSI subgroups have distinct deficits in executive functions suggest that engaging in NSSI might have different functions for different adolescents. This further emphasizes that performing a neuropsychological assessment in a clinical setting might yield clinical information that is

valuable to meet the specific therapeutic needs of the individual adolescent engaging in NSSI. The finding of no deficits with respect to general cognitive functioning further emphazises the importance of performing a neuropsychological assessment with this adolescent group. Normal general cognitive functioning might make it difficult to notice deficits in specific aspects of neuropsychological funtioning, which might be revealed first through a thorough neuropsychological assessment.

Second, a clinical assessment in general and a diagnostic evaluation in particular should be performed with adolescents engaging in NSSI. As reported in paper I, the research findings show that NSSI is associated with symptoms of depression and anxiety as well as heightened levels of both experienced and expressed anger. With respect to psychiatric diagnoses (also reported in paper I) NSSI is particularly associated with MDD, and also there was a tendency for an association with social phobia. Thus, in light of the associations between NSSI and these clinical symptoms and diagnoses, a diagnostic assessment of adolescents engaging in NSSI seems to be of clinical value. As with a neuropsychological assessment, a diagnostic assessment can provide clinical information that is needed to tailor the therapeutic needs to each adolescent struggling with NSSI.

The present research findings also have clinical implications that might be relevant for the treatment of NSSI in adolescents. Research clearly is needed to establish these clinical implications, so for now they can only be considered as preliminary implications. First, as selective deficits in specific aspects of executive functions as well as in specific aspects of verbal learning and memory can represent neuropsychological mechanisms that might be involved in NSSI, training programmes specifically aimed at improving these impaired functions might possibly improve these specific functions and thereby possibly reduce NSSI. At the moment, this possibility certainly only can have the status as a potential implication of

our findings. Still, this possible clinical implication is in accordance with research showing beneficial effects of training working memory on other aspects of executive functions and on ADHD symptoms in children (Klingberg et al., 2005).

Second, the present findings indicate that the impulsive response style in adolescents engaging in NSSI primarily is triggered by stress as when in psychological distress. This might imply that the identification and recognition of factors that elicit psychological distress could be an important therapeutic focus to reduce the occurrence of impulsively engaging in NSSI when in psychological distress. Also, this might imply that the development of more adaptive strategies both for managing stressful situations and for regulating emotions, given that NSSI is engaged in for affect-regulating purposes, should be targeted in therapy.

Third, the finding of low serotonin being involved in the impulsive response style might suggest that the administration of SSRIs might help reduce NSSI in adolescents. This is consistent with research findings showing that SSRIs reduced non-suicidal self harm in adolescents with depression (Goodyer et al., 2007).

Future Perspectives

The present study primarily investigated the reasons why adolescents engage in NSSI within a neuropsychological/biological framework. Further research with other perspectives are needed to reach the overall aim of gaining more knowledge on the reasons why adolescents engage in NSSI.

Since reseach findings suggest a role for executive functions in emotion regulation (Phillips et al., 2003; Schmeichel et al., 2008; Van Dillen & Koole, 2007), the present findings of impaired executive functions in adolescents engaging in NSSI, might suggest that this adolescent group struggles with regulating emotions. However, as we did not include any

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direct measure of emotion dysregulation, the present findings only indirectly can support the emotion regulation hypothesis from a neuropsychological perspective. Nevertheless, in this research project we wanted to test specific executive functions found to be involved in the ability to regulate emotions *per se*. Thus, our investigation of executive functions in this adolescent group was a first reasonable step in increasing knowledge on the emotion regulation hypothesis of NSSI (Jacobsen & Gould, 2007) from a neuropsychological perspective. Surely, future studies further investigating the emotion regulation hypohesis, should include direct measures of emotion dysregulation. Relatedly, future studies are needed to investigate whether this adolescent group also have increased emotional reactivity, which constitutes another important vulnerability for emotional dysregulation (Nock, Wedig, Holmberg, & Hooley, 2008). In close association with this, a recent study found that adolescents engaging in NSSI showed higher physiological reactivity, as measured by skin conductance, during a distressing task as compared with healthy controls (Nock & Mendes, 2008). Still, including specific measures of emotional reactivity in future research are essential to investigate whether adolescents engaging in NSSI also have a vulnerability in this respect, and thus to explore the emotion regulation hypothesis of NSSI even further.

Considering the heterogeneous nature of NSSI (Lloyd-Richardson et al., 2007; Skegg, 2005; Whitlock et al., 2008), we classified the adolescents engaging in NSSI into two NSSI subgroups reflecting low and high severity NSSI, when investigating the aspects of executive functions (paper I). Our procedure for classification was based on a thorough literature review, showing that the the NSSI forms and the number of different NSSI behaviours engaged in are particularly important in distinguishing NSSI severity (Jacobsen & Gould, 2007; Whitlock et al., 2008). However, future studies are needed to further investigate the validity of the NSSI subgroups resulting from this particular classification procedure.

Specifically, such studies should be undertaken to investigate the discriminative validity of these NSSI subgroups, i.e., whether the NSSI subgroups differ in further respects that makes sense theoretically and clinically. The findings from such studies, investigating the discriminative validity of the NSSI subgroups, will in turn either support or discourage further use of this particular classification procedure. Furthermore, considering the heterogeneous nature of NSSI, it would be interesting to explore individual differences within the overall NSSI group in future studies.

A longitudinal study following community sampled preadolescents that never have engaged in any NSSI into adolescence would be of great interest. Such a longitudinal study could involve neuropscyhological testing, clinical evaluations and screening of NSSI at several time points, and thereby help illuminate the chronological associations between deficits in specific aspects of neuropsychological functions, symptoms of psychological disorders as well as onset of engaging in NSSI. Thus, a longitudinal study could help answering whether the deficits in specific aspects of neuropsychological functions are present before onset of engaging in NSSI and thus whether they might represent vulnerabilities for engaging in NSSI or on contrary are concomitants or consequences of engaging in NSSI.

Future research should also focus on the functional consequences of deficits in specific aspects of executive functions as well as in verbal learning and memory in adolescents engaging in NSSI. Considering that adolescence is an important period for the development of long-term patterns of academic functioning (Lerner et al., 1997), one perhaps particularly important focus for future studies is to investigate whether specific neuropsychological deficits are associated with lower academic achievements in adolescents engaging in NSSI. Thus, future neuropsychological studies that include measures of functional consequences in general and academic attainments in particular are needed to specify the connection between

deficits in specific aspects of neuropsychological functions and their functional consequences in this specific adolescent group.

Further studies are also wanted to investigate the effects of ATD on dimensions of impulsivity and mood in healthy adolescent females and males. Findings from such studies are needed to disentangle whether the present effects of ATD on impulsivity and mood are merely age- or sex-dependent, or really represent distinctive qualities in adolescent females engaging in NSSI. Such future studies should also include adolescent males engaging in NSSI to investigate whether there are sex-specific effects of ATD on dimensions of impulsivity and mood in adolescents engaging in NSSI in particular. Studies should also investigate the effects of ATD on impulsivity and mood in adolescents recruited from clinical populations. This will help clarify whether ATD influences dimensions of impulsivity and mood in the same vein in a clinical group as in the present community sampled group of adolescents, thus either supporting or discouraging the external validity of the present findings.

Considering that there are various subtypes of impulsivity (Evenden, 1999; Winstanley et al., 2004), future studies are also needed to investigate additional subtypes of impulsivity in adolescents engaging in NSSI. Performance on behavioural tasks measuring various forms of impulsivity should be assessd both in ordinary neuropsychological test sessions as well as in sessions involving experimental manipulations of level of stress. Findings from such studies might further advance our knowledge both of which specific forms of impulsivity that might be involved in NSSI and of the specific circumstances in which they are apparent or elicited.

Studies on the treatment of NSSI should investigate neuropsychological functions at the start of treatment. By doing so, one could investigate both the prognostic value of neuropsychological variables on the efficacy of various treatments as well as the effects on neuropsychological functions of the various treatments offered to this specific adolescent group.

Conclusions

One main finding of the present study is that NSSI subgroups have distinctive deficits in executive functions. The high-severity NSSI group has working memory deficits, while the low-severity NSSI group has impaired inhibitory control. This indirectly supports the emotion regulation hypothesis. Another main finding is that adolescents engaging in NSSI exhibit impairments in verbal learning and memory. The core problems involve impaired short-term memory/working memory and difficulty in the encoding of material into long-term memory. This suggests that an inefficient network comprising frontal cortex and more posterior structures are involved in NSSI. Following ATD, female adolescents engaging in NSSI adopted a focused and directed impulsive response style. This findings might suggest that low serotonin function triggers this particular group of female adolescents to impulsively engage in NSSI when in emotional distress. This might possibly be relevant for emotion regulation in female adolescents engaging in NSSI.

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Papers I-III

I

Executive functions are impaired in adolescents engaging in non-suicidal self-injury

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Background. The aim of this study was to investigate three main aspects of executive functions (EFs), i.e. shifting, updating and inhibition, in adolescents engaging in non-suicidal self-injury (NSSI) as compared with healthy controls.

Method. EFs were assessed using the Intra/Extradimensional Set Shift, the Spatial Working Memory (SWM) Test and the Stop Signal Test (SST) from the Cambridge Neuropsychological Test Automated Battery (CANTAB), in a high-severity NSSI group ($n = 33$), a low-severity NSSI group ($n = 29$) and a healthy control group ($n = 35$). Diagnostic characteristics were examined using the Kiddie-Sads-Present and Lifetime Version.

Results. There were group differences on the SWM Test. A trend towards an interaction effect of sex revealed that males in the high-severity NSSI group made significantly more errors than males and females in the control group. Both males and females in the high-severity NSSI group made poor use of an efficient strategy in completing the test. The low-severity NSSI group performed poorly on the SST, making more errors than the control group and showing an impaired ability to inhibit initiated responses, as compared with the high-severity NSSI group. There were group differences in frequencies of current and previous major depressive disorder. However, no effects of these diagnoses were found on any of the EF tests.

Conclusions. This study demonstrates that NSSI subgroups have distinct deficits in EFs. The high-severity NSSI group has working memory deficits, while the low-severity NSSI group has impaired inhibitory control. This supports the emotion regulation hypothesis.

Introduction

Non-suicidal self-injury (NSSI) is alarmingly widespread in community samples of adolescents (Ross & Heath, 2002; Zoroglu *et al.* 2003; Muehlenkamp & Gutierrez, 2004, 2007). NSSI involves the deliberate, direct destruction or alteration of body tissue with no conscious suicidal intent (Favazza, 1998; Lloyd-Richardson *et al.* 2007). NSSI is heterogeneous, ranging from minor to severe forms (Lloyd-Richardson *et al.* 2007; Whitlock *et al.* 2008) and NSSI behaviours can be classified into subgroups based on their potential for causing tissue damage (Skegg, 2005; Whitlock *et al.* 2008). Some find higher prevalence rates in girls than in boys (see, for instance, Ross & Heath, 2002), whereas others find no sex difference (see, for instance, Muehlenkamp & Gutierrez, 2004). Sex

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differences in forms and numbers of NSSI behaviours engaged in exist (Whitlock *et al.* 2008).

According to the emotion regulation hypothesis, adolescents engage in NSSI to regulate their emotions, most often to decrease their negative affective states (Jacobson & Gould, 2007). This is supported by findings showing that prior to engaging in NSSI, adolescents experience negative emotions, such as anger, sadness and anxiety, which are reduced during and especially after having self-injured (Ross & Heath, 2003; Laye-Gindhu & Schonert-Reichl, 2005). However, these findings are exclusively based on adolescents' retrospective self-reports (Jacobson & Gould, 2007). This confirms the need for exploring the emotion regulation hypothesis in a more objective manner.

In a model of the neural basis of emotion processing, two neural systems underlie neuropsychological processes that are important for emotional behaviour (Phillips *et al.* 2003). The ventral system, including the amygdala, insula, ventral striatum, and ventral

regions of the anterior cingulate gyrus and prefrontal cortex, is primarily important for the identification of the emotional significance of a stimulus, the ensuing production of an affective state, and the automatic regulation of emotional responses. The dorsal system includes the hippocampus and dorsal regions of anterior cingulate gyrus and prefrontal cortex. It is important for the performance of executive functions (EFs), which includes effortful regulation of affective states and emotional behaviours. This involves an inhibition or modulation of the processes that are mainly dependent upon the ventral system (Phillips *et al*. 2003). Thus, impaired EFs suggest an ineffective ability to regulate emotions. EFs may be defined as the skills that are essential for purposeful, goal-directed activity (Anderson, 1998). Although the different EFs are interrelated, they are meaningfully diverse abilities (Miyake *et al*. 2000). Shifting between mental sets or tasks, updating and monitoring of information in working memory (WM), and inhibition of dominant responses are main aspects of EFs (Miyake *et al*. 2000). Although not completely consistent (Herba *et al*. 2006), some find sex differences in EFs in adolescents (Anderson *et al*. 2001; Fields *et al*. 2009).

Only three studies have previously examined neuropsychological functions in adolescents engaging in self-injuring behaviours. No differences were found between adolescents and adults engaging in NSSI as compared with controls on measures of impulsivity (Janis & Nock, 2009). Likewise, no differences were found between adolescents engaging in self-injurious behaviours and adolescents with none such behaviours on tests of EFs (Ohmann *et al*. 2008). However, adolescents who currently self-harmed showed impaired decision making compared with adolescents with a previous history of self-injuring, adolescents with depression and healthy controls (Oldershaw *et al*. 2009).

The primary aim of the present study was to explore the main aspects of EFs – shifting, updating and inhibition – in adolescents engaging in NSSI. Since adolescents engaging in NSSI constitute a heterogeneous group, we examined a high-severity NSSI group, a low-severity NSSI group in addition to a control group along these basic dimensions of EFs. As there may be sex differences in NSSI and EFs, we investigated the possible interactive effect of sex.

Method

Participants

A total of seventeen high schools in urban and nearby areas agreed to participate in the study. All grade 9 students present at the schools at the scheduled

times were approached to participate. A total of 327 adolescents were recruited and participated in the screening session. Group sizes of approximately 30 adolescents would enable us to detect group differences (Kyte *et al*. 2005; Matthews *et al*. 2008). To ensure such group sizes in the test session, we screened until we had 74 adolescents meeting the criteria for inclusion in the NSSI subgroups. The control group, matched as closely as possible for sex, ethnicity and school belonging, was randomly selected from those who had never engaged in any NSSI. This resulted in 116 adolescents being selected to participate in the test session (74 adolescents in the NSSI subgroups and 42 adolescents in the control group). As 13 of these withdrew from further participation, this left 103 adolescents participating in the test session. Based on participants' reported NSSI in the screening questionnaire and in the section on NSSI in the semi-structured diagnostic interview in the test session, participants were classified into three groups: a high-severity NSSI group ($n=33$), a low-severity NSSI group ($n=29$) and a control group ($n=35$). Of participants that had reported that they had never engaged in NSSI on the screening questionnaire, five revealed in the interview that they had engaged in one NSSI behaviour during the past year. They were excluded from all analyses as they failed to meet the criteria for any of the groups. Furthermore, due to extreme scores on several measures, one girl in the control group was excluded from all analyses.

NSSI was defined as the deliberate, direct destruction or alteration of body tissue with no conscious suicidal intent. Acts such as mentally hurting oneself and engaging in risky behaviours were excluded. Inclusion in the NSSI subgroups required that the adolescent had engaged in at least two different NSSI behaviours during the past year. Participants meeting these initial criteria were given a score reflecting the severity of their NSSI. Two NSSI characteristics were used to calculate the NSSI severity score; the form(s) and the total number of different NSSI behaviours engaged in.

With respect to NSSI forms, NSSI behaviours were classified into three groups based on their potential for causing tissue damage (Skegg, 2005; Whitlock *et al*. 2008). Behaviours with potential for superficial tissue damage were each scored 1, while those with potential for causing bruising or light tissue damage were each scored 2. Last, behaviours with potential for causing severe tissue damage were each scored 3.

To ensure reliability of the classification of NSSI behaviours into the three groups, training of two raters was completed, resulting in 90% agreement on 20% of the data. Table 1 summarizes the classification of NSSI behaviours into the three groups. For each

Table 1. *The categorization of NSSI behaviours into three groups*

Superficial tissue damage (each scores 1)	Bruising and light tissue damage (each scores 2)	Severe tissue damage (each scores 3)
Picking at a wound	Hitting oneself	Cutting or carving one's skin
Biting oneself	Pulling one's hair out	Giving oneself a tattoo
Picking areas of one's body to the point of drawing blood	Inserting objects under one's nails or skin	Burning
Scraping one's skin		Erasing one's skin

NSSI, Non-suicidal self-injury.

participant meeting the initial criteria for inclusion in the NSSI subgroups, the weighted scores of the NSSI behaviours were summarized to give an NSSI severity score (mean = 7.9, S.D. = 3.6, median = 7.0).

The median was used as the cut-off point separating the participants into the two NSSI subgroups. Of the participants, nine scored this value. Of these, five were classified into the high-severity NSSI group as they had engaged in NSSI behaviours in all three NSSI groups, a similar pattern to the majority (i.e. 25 of 28) of participants in the high-severity NSSI group. The four remaining participants were classified into the low-severity NSSI group as they had engaged in NSSI behaviours in two NSSI groups, either groups 1 and 2 or groups 1 and 3, a similar pattern to the majority (i.e. 20 of 25) of participants in the low-severity NSSI group. Table 2 summarizes the number of participants having engaged in each NSSI behaviour and in each combination of different NSSI groups, separately for each NSSI subgroup.

The study was carried out in accordance with the Helsinki Declaration and accepted by the local regional ethics committee.

Measures

Symptom assessment

Functional Assessment of Self-Mutilation (*FASM*). The FASM (Lloyd *et al*. 1997, cited by Lloyd-Richardson *et al*. 2007) is a self-report questionnaire of the methods, frequency and functions of NSSI. Studies with adolescent samples have yielded support for its psychometric properties (Nock & Prinstein, 2005; Lloyd-Richardson *et al*. 2007).

Kiddie-Sads – Present and Lifetime Version (*K-SADS-PL*). The K-SADS-PL (Kaufman *et al*. 1997) is a semi-structured diagnostic interview assessing current and lifetime history of psychopathology in children and adolescents according to DSM-IV criteria (APA, 1994). The following diagnoses were considered particularly relevant and were examined: major depressive disorder (MDD), generalized anxiety, obsessive compulsive disorder, panic disorder, social phobia, post-traumatic stress disorder, anorexia nervosa, bulimia nervosa, attention deficit hyperactivity disorder, alcohol abuse and substance abuse.

Beck Depression Inventory (*BDI*). The BDI (Beck *et al*. 1988*b*) is a 21-item self-report measure of depressive symptoms. Its psychometric properties for use with adolescents are supported (Larsson & Melin, 1990; Ambrosini *et al*. 1991).

Beck Anxiety Inventory (*BAI*). The BAI (Beck *et al*. 1988*a*) is a 21-item self-report measure of anxiety. It shows acceptable psychometric properties in adolescent samples (Jolly *et al*. 1993; Osman *et al*. 2002).

State-Trait Anger Expression Inventory (*STAXI*). The STAXI (Spielberger, 1988) is a self-report measure of the experience and expression of anger. It has been used with adolescents (Guertin *et al*. 2001). Its subscales have adequate internal consistency and construct validity (Spielberger, 1988).

Neuropsychological tests

Wechsler Abbreviated Scale of Intelligence (*WASI*). The WASI (Psychological Corporation, 1999) provides a brief estimate of intelligence. It consists of four subtests: vocabulary, block design, similarities, and matrix reasoning. The primary variables of interest were the total intelligence quotient (IQ) score and the IQ sum scores on the verbal and non-verbal tests, respectively.

Cambridge Neuropsychological Test Automated Battery (*CANTAB*). Tests were selected from the Cambridge Neuropsychological Test Automated Battery (CANTAB; Cambridge Cognition, 2006): obligatory training tests and EF tests.

Table 2. *The number of participants having engaged in each NSSI behaviour and in each combination of different NSSI groups, separately for each NSSI subgroup*

	Low-severity NSSI ($n=29$)	High-severity NSSI ($n=33$)	Sum ($n=62$)
Superficial tissue damage			
Picking at a wound	18	24	42
Biting oneself	13	24	37
Picking areas of one's body to the point of drawing blood	6	11[a]	17[a]
Scraping one's skin	17	21	38
Other (e.g. scratching oneself, sticking oneself with a needle)	9	14	23
Bruising and light tissue damage			
Hitting oneself	10[b]	19[b]	29[c]
Pulling one's hair out	3	12	15
Inserting objects under one's nails or skin	1	3	4
Other (e.g. pinching oneself, pulling one's hair)	5	9	14
Severe tissue damage			
Cutting or carving one's skin	12[b]	28	40[b]
Giving oneself a tattoo	0	7	7
Burning	2	8	10
Erasing one's skin	0	12	12
Other	0	0	0
Combinations of different NSSI groups engaged in			
Superficial tissue damage only	3	0	3
Superficial tissue damage + bruising and light tissue damage	13	0	13
Superficial tissue damage + severe tissue damage	11	3	14
Superficial tissue damage + bruising and light tissue damage + severe tissue damage	2	30	32

NSSI, Non-suicidal self-injury.
[a] Three scores missing.
[b] One score missing.
[c] Two scores missing.

The obligatory training tests administered were The Motor Screening test (MOT) and Big/Little Circle (BLC), which are training tests administered in advance of other CANTAB tests.

Each of the three EF tests administered measures each of the main aspects of EFs, i.e. shifting, updating and inhibition (Miyake *et al*. 2000).

The Intra/Extradimensional (IED) Set Shift measures shifting. The subject must learn which of two presented stimuli is correct, assisted by feedback from the computer. Initially, two stimuli of one dimension (pink shapes) are shown, then each of two dimensions (pink shapes and white lines) are shown. The stimuli and/or rules change after six consecutive correct responses (the criterion of learning at each stage). These shifts are initially intra-dimensional (pink shapes are the relevant dimension), then extra-dimensional (white lines become the relevant dimension). The test terminates if at any stage the subject fails to reach the criterion of learning after 50 trials. The variables of interest were: stages completed, pre-ED errors and EDS errors. These reflect the number of stages completed successfully, the number of errors made prior to the extra-dimensional shift and in the extra-dimensional stage of the task, respectively.

The Spatial Working Memory (SWM) test measures updating and monitoring of spatial information in WM. The screen displays a number of boxes. The subject has to find one token in each box and use them to fill up a column on the side of the screen. Gradually, the number of boxes increases from three to eight. Touching any box where a token has already been found is an error. The subject decides the order in which boxes are visited. The variables of interest were total errors and strategy, reflecting the number of errors made and the use of an efficient strategy for completing the task, respectively.

The Stop Signal Task (SST; Logan *et al.* 1984) measures inhibition of dominant responses. The screen shows a white ring, in which a left- or right-pointing arrow is displayed. First, the subject has to press the left button on a press pad when seeing a left-pointing arrow, and the right button when seeing a right-pointing arrow. In the second part of the task, the subject has to continue pressing the buttons as before, but has to withhold pressing the button if hearing a beep. The variables of interest were direction errors on stop and go trials and stop signal reaction time (SSRT) last half, expressing the number of times the subject pressed the wrong button and the ability to inhibit an initiated response (Eagle *et al.* 2007), respectively.

Procedure

A researcher met all potential participants in their classrooms, informing them about the study. The adolescents also received written information, including information to their parents. Before participation, all participants and their parents signed an informed consent. The participants were seen in two sessions.

Screening session

The participants from each school completed the FASM in a classroom. On the basis of their responses to the FASM, participants meeting the criteria for inclusion in the NSSI subgroups were identified.

Test session

All participants met at the Department of Psychology at the University in Oslo. They completed the following tests: MOT, BLC, IED, SWM, SST and WASI. They also completed BDI, BAI and STAXI. A clinical psychologist administered the sections covering the selected psychiatric diagnoses in K-SADS-PL. All participants were tested individually and were compensated 25 Euros for their participation.

Statistical analysis

SPSS for Windows (version 16.0; SPSS Inc., USA) was used to register and analyse data. To assess group differences in depressive and anxious symptoms and anger, one-way between-groups analyses of variance (ANOVA) were completed. Group comparisons in frequencies of each diagnosis were performed using χ^2 tests.

Scores on the dependent variables on the three EF tests were converted to Z scores. In doing so, we were able to make mean Z scores, reflecting the mean scores of the variables on each EF test for each participant;

one for the IED test variables, one for the SWM test variables and one for the SST variables. When positive scores on the dependent variables on the EF tests had opposite meanings in their interpretation, some of them were reversed accordingly.

In instances of group differences in frequencies of diagnoses, one-way between-groups ANOVA were conducted to explore the main effects of the particular diagnoses on the mean Z score of the variables on each EF test.

To explore main effects of group and sex and their possible interaction on the mean Z score of the variables on each EF test, two-way between-groups ANOVA were performed. Only when these initial analyses yielded significant effects, further two-way ANOVA with scores on each variable on the relevant EF test were completed. *Post-hoc* comparisons using the least significant difference (LSD) test were applied. When interaction effects between group and sex were found, *post-hoc* comparisons were applied using a dummy variable with six values representing the six possible combinations of sex and group (2×3).

As a criterion of statistical significance, an α level of $p < 0.05$ was used. Results reaching trend level (defined as $p < 0.1$) on main or interaction effects are included and commented on.

Results

Demographic, psychometric and clinical characteristics

Table 3 summarizes group demographic, psychometric and clinical characteristics. For two girls in the low-severity NSSI group, current MDD and previous generalized anxiety, respectively, were scored as missing as sufficient information was not obtained in the diagnostic interview. There were no significant group differences in age, sex ratios or on any IQ indicators.

There were significant group differences on the BDI score [$F(2, 94) = 21.16$, $p = 0.00$, $\eta^2 = 0.31$]; the high-severity NSSI group had a higher score than the low-severity NSSI group ($p = 0.00$) and the control group ($p = 0.00$), respectively. The low-severity NSSI group showed a higher score than the control group ($p = 0.00$).

The score on the BAI showed significant group differences [$F(2, 94) = 11.20$, $p = 0.00$, $\eta^2 = 0.19$]; the high-severity NSSI group had a higher score than both the control group ($p = 0.00$) and the low-severity NSSI group ($p = 0.00$).

There were significant group differences on the STAXI trait score [$F(2, 94) = 16.70$, $p = 0.00$, $\eta^2 = 0.26$];

Table 3. *Demographic, psychometric and clinical characteristics*

	Healthy controls (*n*=35)	Low-severity NSSI (*n*=29)	High-severity NSSI (*n*=33)
Sex, *n* (%)			
Female	25 (71.4)	22 (75.9)	26 (78.8)
Male	10 (28.6)	7 (24.1)	7 (21.2)
Age, years	14.7 (0.4)	14.7 (0.5)	14.8 (0.4)
Total IQ	100.0 (12.6)	95.6 (11.8)	95.4 (15.3)
Verbal IQ	96.3 (12.7)	93.3 (12.1)	93.8 (14.6)
Non-verbal IQ	104.0 (13.8)	99.0 (12.6)	97.4 (16.4)
BDI	2.6 (3.0)	7.0 (5.2)	11.1 (7.2)
BAI	4.1 (5.0)	6.3 (5.9)	11.3 (8.0)
STAXI			
Trait	17.0 (4.0)	20.0 (5.9)	25.3 (7.7)
State	10.3 (1.0)	10.8 (1.8)	11.0 (3.2)

NSSI, Non-suicidal self-injury; IQ, intelligence quotient; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; STAXI, State-Trait Anger Expression Inventory.

Values are given as mean (standard deviation) unless otherwise indicated.

the high-severity NSSI group showed a higher score than both the control ($p=0.00$) and the low-severity NSSI group ($p=0.00$), respectively. Also, the low-severity NSSI group had a higher score than the control group ($p=0.05$). No significant group differences were found on the STAXI state score.

There were no significant group differences in frequencies of any diagnoses with the exception of current MDD (control group=0%, low-severity NSSI group=10.7%, high-severity NSSI group=21.2%, $\chi^2=8.19$, df=2, $p<0.02$) and previous MDD (control group=0%, low-severity NSSI group=0%, high-severity NSSI group=15.2%, $\chi^2=10.22$, df=2, $p<0.01$). However, there was a trend towards significant group differences on current social phobia (control group=0%, low-severity NSSI group=3.4%, high-severity NSSI group=12.1%, $\chi^2=5.35$, df=2, $p<0.07$).

No main effects of either current or previous MDD on the mean Z scores of the IED variables, the SWM variables or the SST variables, respectively, were found. Accordingly, they were not included in further analyses.

Performance on EF tasks

Table 4 summarizes performance on all EF tasks, displayed by each group and separately for males and females in each group. Fig. 1 depicts group differences in scores on the SSRT.

IED variables

No significant group or sex differences or any interaction effect between group and sex were found on the mean Z score of the IED variables.

SWM variables

On the mean Z score of the SWM variables, there were significant group differences [$F(5, 91)=3.98$, $p=0.02$, $\eta^2=0.08$]. There were no significant sex difference or interaction effect between group and sex. *Post-hoc* comparisons revealed no significant group differences.

Significant group differences were found on the SWM total error score [$F(5, 91)=4.08$, $p=0.02$, $\eta^2=0.08$], but no sex difference was found. There was a trend towards a significant interaction effect between group and sex [$F(5, 91)=2.75$, $p=0.07$, $\eta^2=0.06$]. A scatter plot inspection of these results revealed that the significant main effect of group was caused by the interaction effect of sex. *Post-hoc* comparisons showed that males in the high-severity NSSI group had a higher score than both males ($p=0.00$) and females in the control group ($p=0.03$).

On the SWM strategy score, there were significant group differences [$F(5, 91)=3.52$, $p=0.03$, $\eta^2=0.07$]; the high-severity NSSI group had a higher score than the low-severity NSSI group ($p=0.04$). No significant sex difference or interaction effect between group and sex emerged.

Table 4. *Summary of results on all executive function tasks in each group and separately for males and females in each group*

	Healthy controls			Low-severity NSSI			High-severity NSSI		
	Total	Males	Females	Total	Males	Females	Total	Males	Females
IED									
Stages completed	8.4 (0.9)	8.6 (0.8)	8.4 (0.9)	8.3 (0.9)	9.0 (0.0)	8.1 (1.0)	8.6 (0.8)	8.7 (0.5)	8.5 (0.9)
Pre-ED errors	6.5 (1.8)	6.9 (1.4)	6.3 (2.0)	6.8 (2.7)	9.1 (3.3)	6.1 (2.1)	8.1 (3.5)	8.0 (2.0)	8.1 (3.8)
EDS errors	12.7 (10.4)	8.3 (8.9)	14.4 (10.5)	12.5 (12.0)	2.9 (2.3)	15.5 (12.3)	10.0 (9.6)	11.4 (8.5)	9.6 (9.9)
SWM									
Strategy	30.0 (4.7)	28.1 (4.5)	30.8 (4.6)	29.3 (5.9)	27.4 (6.3)	30.0 (5.8)	32.1 (5.0)	33.4 (5.7)	31.7 (4.9)
Total errors	14.8 (12.7)	10.0 (11.6)	16.7 (12.8)	19.1 (13.0)	19.0 (10.1)	19.1 (14.0)	20.8 (13.6)	29.0 (8.2)	18.5 (14.1)
SST									
Direction errors[a]	5.0 (7.1)	4.4 (4.9)	5.2 (7.9)	9.5 (11.3)	15.7 (14.2)	7.6 (9.7)	5.7 (5.7)	7.1 (5.7)	5.3 (5.8)
SSRT	187.7 (48.4)	198.4 (55.9)	183.5 (45.6)	212.0 (60.5)	250.5 (76.7)	199.8 (50.4)	173.3 (39.8)	174.5 (21.4)	173.0 (43.8)

NSSI, Non-suicidal self-injury; IED, Intra-Extradimensional Set Shift; Pre-ED errors, errors made prior to the extra-dimensional shift; EDS errors, errors made in the extra-dimensional stage; SWM, Spatial Working Memory; SST, Stop Signal Task; SSRT, Stop Signal Reaction Time.

Values are given as mean (standard deviation).

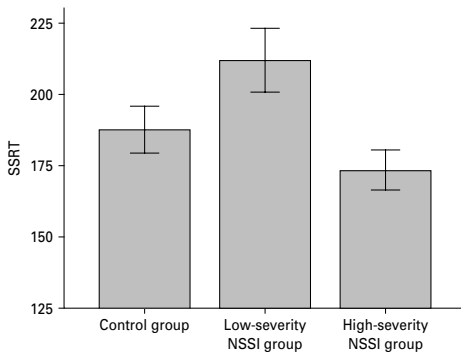[a] Direction errors on stop and go trials.

Fig. 1. Scores on the Stop Signal Reaction Time (SSRT) for the three groups. Values are means, with standard errors represented by vertical bars. NSSI, Non-suicidal self-injury.

SST variables

On the mean Z score of the SST variables, there were significant group differences [$F(5, 91) = 6.26$, $p = 0.00$, $\eta^2 = 0.12$]; the low-severity NSSI group had higher scores than the control group ($p = 0.02$) and the high-severity NSSI group ($p = 0.01$), respectively.

A trend towards a sex difference [$F(5, 91) = 3.91$, $p = 0.05$, $\eta^2 = 0.04$] was found, while no interaction effect between group and sex emerged.

On the score on SST direction errors on stop and go trials, there were significant group differences [$F(5, 91) = 4.61$, $p = 0.01$, $\eta^2 = 0.09$]; the low-severity

NSSI group had a higher score than the control group ($p = 0.03$). There were no sex difference or interaction effect between group and sex.

There were significant group differences on the score on the SSRT variable [$F(5, 91) = 6.21$, $p = 0.00$, $\eta^2 = 0.12$]; the low-severity NSSI group had a higher score than the high-severity NSSI group ($p = 0.00$). A trend towards a sex difference emerged [$F(5, 91) = 3.71$, $p = 0.06$, $\eta^2 = 0.04$], while no interaction effect between group and sex was found.

Discussion

The main finding in this study was that the high-severity NSSI had WM deficits, while the low-severity NSSI group had impaired inhibitory control. There were no significant group differences in IQ, strengthening the conclusion that the results reflect impairments in specific aspects of EFs and not group differences in general cognitive abilities. Neither NSSI subgroups had shifting deficits.

The males in the high-severity NSSI group made particularly many errors on the WM task, emphasizing the importance of examining interaction effects of sex. Nevertheless, the females in the high-severity NSSI group also had WM deficits, as shown in their poor use of the efficient strategy in completing the task. Males in the low-severity group had the most impaired inhibitory control; however, the females in the same group showed the same pattern.

Our findings replicate previous findings of associations between NSSI and depressive (Ross & Heath,

2002; Laye-Gindhu & Schonert-Reichl, 2005) and anxious symptoms (Ross & Heath, 2002) and anger control problems (Laye-Gindhu & Schonert-Reichl, 2005). Those meeting criteria for a current or a previous MDD did not perform worse on the EF tests than those who did not meet the criteria. This indicates that impairments in EFs in adolescents engaging in NSSI are not just an expression of an underlying psychological disorder.

The adolescents in the high-severity NSSI group had WM deficits, suggesting that their ability to distract themselves to regulate negative moods is impaired. By loading WM with tasks demanding effortful cognitive processing, mood-congruent processing can be prevented and thereby result in distraction from negative moods (Van Dillen & Koole, 2007). In this way WM is one mechanism through which distraction from negative moods operates (Van Dillen & Koole, 2007) and is thereby related to emotion regulation.

Following a predetermined search sequence is an efficient strategy in completing the WM task (Owen *et al*. 1990). The poor use of this strategy among adolescents in the high-severity NSSI group suggests that they struggle in focusing on a specific strategy, reflecting a fundamental deficit in their use of organizational strategies (Owen *et al*. 1990). This might complicate their strategically loading of WM with mood-incongruent processing, and thereby impair their ability to distract themselves from negative moods. Previous findings show a positive association between strategy score and number of errors (Owen *et al*. 1990). For the males in the high-severity NSSI group, the poor use of the efficient strategy may explain the many errors they made. However, this does not apply for the females, making no more errors than the other groups. This is difficult to explain. Using the efficient strategy may reduce the loading on WM (Owen *et al*. 1990). Apparently females in the high-severity NSSI group can complete tasks requiring WM, but due to ineffective organizational strategies, their WM becomes 'overloaded'. This could impair their ability to distract themselves from negative moods.

Another mechanism through which emotion regulation occurs is suppression, demanding inhibition of prepotent responses (Nash *et al*. 2007). Although suppression does not provide relief from negative emotions, it can inhibit emotional behavioural expression (Gross & Levenson, 1997). In light of the emotion regulation hypothesis, it is surprising that the high-severity NSSI group did not have impaired inhibitory control. In contrast, the impaired inhibitory control found in the low-severity NSSI group might suggest an impaired ability to suppress emotional behavioural expressions of negative emotions.

Our finding of no impaired inhibitory control in the high-severity NSSI group implies that their self-injuring is not engaged in impulsively. Although engaging in similar NSSI behaviours, the high-severity NSSI group may engage in NSSI behaviours in a more deliberate, self-injuring way than the low-severity NSSI group. This is consistent with previous research showing that adolescents engaging in moderate/severe NSSI are likely to contemplate NSSI before engaging in the behaviour (Lloyd-Richardson *et al*. 2007).

In contrast, the impaired inhibitory control in the low-severity NSSI group suggests an impulsive nature of their self-injuring. As there are individual differences in the degree to which adolescents engage in emotion-based rash action and risky behaviour (Cyders & Smith, 2008), the adolescents in the low-severity NSSI group might be on the one extreme on this disposition. Accordingly, their self-injuring might primarily reflect benign, clinically insignificant experimenting with these behaviours. This is in contrast to the self-injuring nature of the same behaviours, reflecting pathological, clinically significant NSSI among the adolescents in the high-severity NSSI group.

With one exception (Oldershaw *et al*. 2009), our main findings are inconsistent with previous findings of no impaired EFs in adolescents engaging in NSSI. There are several possible explanations for the inconsistency. First, previous studies have only had one NSSI group. As adolescents engaging in NSSI represent a heterogeneous group (Lloyd-Richardson *et al*. 2007; Whitlock *et al*. 2008), we classified them into subgroups, thereby finding distinctive features for each group. Furthermore, the use of different EF tests can explain the inconsistency. The theoretically driven tests used in our study accurately measure each main aspect of EFs (Robbins *et al*. 1998; Miyake *et al*. 2000) and can detect specific impairments in adolescent populations (Fagerlund *et al*. 2006; Matthews *et al*. 2008). Last, self-injury has been defined differently across studies, possibly influencing the findings.

The behaviours that qualify for NSSI and those that are of clinical significance are unresolved issues (Lloyd-Richardson *et al*. 2007). We decided to use as criteria for inclusion in the NSSI subgroups that the adolescents had engaged in at least two different NSSI behaviours during the past year because, first, this would exclude adolescents only endorsing the item 'picked at a wound', as it in isolation may reflect non-pathological, non-NSSI (Lloyd-Richardson *et al*. 2007). Second, previous studies (Ross & Heath, 2002; Laye-Gindhu & Schonert-Reichl, 2005) have included adolescents having only engaged in one NSSI behaviour as self-injurers. Thus, our criteria did not seem too

liberal. Third, in a community sample of adolescents, the mean number of different NSSI behaviours performed was 2.35 (Lloyd-Richardson *et al.* 2007). Our criteria could not be too conservative relative to this finding, i.e. it should capture the average adolescent engaging in NSSI in a community sample.

Furthermore, our procedure for classifying adolescents into the NSSI subgroups was based on a thorough literature review. The NSSI forms and the number of different NSSI behaviours engaged in are particularly important in distinguishing NSSI severity (Jacobson & Gould, 2007; Whitlock *et al.* 2008). NSSI frequency was not included in quantifying NSSI severity for two reasons. First, its association with severity is unclear (Jacobson & Gould, 2007). Second, frequency of NSSI is difficult to assess retrospectively (Jacobson & Gould, 2007). In accordance with this, a substantial number of the adolescents in our study claimed that they did not know or could not remember how many times they had engaged in NSSI. Thus, we found NSSI frequency to be a too unreliable criterion for NSSI severity.

The relatively few males in our sample raises the question of the reliability of our findings. By interpreting our findings as reflecting real group differences, there is a risk of committing a type I error. However, rejecting our findings entails the possibility of committing a type II error. The risks of ignoring our findings of impairments in EFs in adolescents self-injuring seem substantial. However, the reliability of our findings will be strengthened if replicated with samples including more males. Furthermore, it would be interesting to explore individual differences within the NSSI subgroups in future studies.

In addition to impaired EFs, increased emotional reactivity can constitute a vulnerability for emotional dysregulation (Nock *et al.* 2008). Heightened levels of activity within the ventral system may be associated with increased emotional reactivity, resulting in abnormalities in emotional regulation (Phillips *et al.* 2003). Including a measure of emotional reactivity in future research may inform us whether adolescents engaging in NSSI also have a vulnerability in this respect.

In conclusion, NSSI subgroups have distinct deficits in EFs, supporting the emotion regulation hypothesis.

Acknowledgements

Declaration of Interest

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