Are neurocognitive factors associated with repetition of self-harm? A systematic review.

Author names and affiliations:

Angharad N. de Cates*[1,2], Karen Rees[3], Fabrice Jollant[4,5], Benjamin Perry[1,2], Karina Bennett[6], Katie Joyce[6], Eimear Leyden[7], Catherine Harmer[8], Keith Hawton[9], Kees van Heeringen[10], Matthew R. Broome[8,11]

[1]Unit of Mental Health and Wellbeing, Warwick Medical School, University of Warwick, UK

[2]Coventry and Warwickshire Partnership NHS Trust, Coventry, UK

[3]Division of Health Sciences, Warwick Medical School, University of Warwick, UK

[4]McGill University, Department of Psychiatry & Douglas Mental Health University Institute, McGill Group for Suicide Studies, Montréal (Québec), Canada

[5]Academic Hospital (CHU) of Nîmes, France

[6]Warwick Medical School, University of Warwick, UK

[7]University Hospitals of Coventry and Warwickshire, Coventry, UK

[8]Department of Psychiatry, University of Oxford, UK

[9]Centre for Suicide Research, Department of Psychiatry, University of Oxford, UK

[10]Unit for Suicide Research, Department of Psychiatry and Medical Psychology, Ghent University, Ghent, Belgium

[11]Oxford Health NHS Foundation Trust, Oxford, UK

[1]*Corresponding author

Corresponding author details:

Angharad N. de Cates

Unit of Mental Wellbeing, Warwick Medical School, University of Warwick, CV4 7AL, United Kingdom

Email address: A.de-Cates@warwick.ac.uk

Fax number: +44(0)2476321528 (clinical secretary)

Abstract

Background:

Prediction of self-harm is limited clinically. Early identification of individuals likely to repeat self-harm could improve outcomes and reduce suicide risk. Various neurocognitive deficits have been found in people who self-harm, but the ability of these to predict repetition has yet to be established

Aims:

Identify neurocognitive factors that may predict repetition of self-harm.

Methods:

Systematic narrative review of English language publications assessing neurocognitive functioning and self-harm repetition, searching multiple databases from inception to March 2015. Quality of studies was appraised. A narrative synthesis was performed.

Results:

7026 unique records were identified, and 169 full-texts assessed. 15 unique studies provided data. No imaging studies could be included. Most studies assessed cognitive control or problem solving, but neither factor was consistently associated with repetition. However, specific tasks may show promise. Two studies in adolescents suggest that value-based decision-making impairments could be predictive of repetition. There were too few results for memory to draw specific conclusions.

Conclusions:

Selected studies suggest promise for particular neurocognitive factors and specific cognitive tasks in terms of repetition of self-harm.

Keywords / Indexing terms

Self-harm

Suicide

Neurocognition

Decision-making

Cognitive control

Executive functioning

Memory

Problem solving

Repetition

Neuroimaging

1. Introduction

1.1 What is self-harm and why is it important to predict repetition?

Self-harm, where an individual intentionally causes physical harm to themselves by self-injury or self-poisoning irrespective of motivation (NICE, 2011), affects those with and without previously diagnosed mental illness. One of the most widely used definitions for research is that proposed by the WHO, where it is described as:

> *…an act with nonfatal outcome, in which an individual deliberately initiates a non-habitual behaviour that, without intervention from others, will cause self-harm,…and which is aimed at realizing changes which the subject desired via the actual or expected physical consequences.*
>
> From (Platt et al., 1992) p192

Self-harm can be associated with significant subsequent morbidity, and it is the key risk factor for future suicide (Carroll et al., 2014). Suicide is the known cause of death for approximately 800,000 people around the world each year, and by 2020, it may equal 2% of the global burden of disease (WHO, 2012). At least 10% of young people report at least one episode of self-harm (Hawton, 2012). The highest rates of self-harm are in females aged 15-24 years (Hawton et al., 2015). Suicide is currently the most common cause of death for young adult males (NCISH, 2015).

1.2 What do we currently understand predicts self-harm and repetition?

With every self-harm episode, the risk of eventual suicide increases (Zahl and Hawton, 2004); the same is true for personal and healthcare costs (Sinclair et al., 2011). Repetition of self-harm is associated with various demographic and clinical factors, such as young age, low educational level (Christiansen and Jensen, 2007; De Leo et al., 2001), unemployment (Tejedor et al., 1999) and certain mental

disorder diagnoses (personality disorder (Blasco-Fontecilla et al., 2009), depression (Hawton et al., 1999), and substance and alcohol misuse (Cooper et al., 2013; Monnin et al., 2012)). However, prediction of self-harm and suicide completion on the sole basis of known risk factors is difficult. For instance, the SADPERSONS tool, a risk assessment based on recognised demographic and clinical factors, does not predict individuals requiring psychiatric admission or community aftercare, or those who repeat self-harm (Quinlivan et al., 2016; Saunders et al., 2014). Currently, the most important predictor of future self-harm and suicide is past self-harm (Carroll et al., 2014; Owens et al., 2002). However, most people who self-harmed will not re-attempt and will not die by suicide (Owens et al., 2002). Therefore, the predictive value of clinical and demographic parameters alone is weak, and in light of the increasing incidence of suicide, assessment using additional factors is required to accurately predict future self-harm. As at least 40% of cases who died from suicide had previously attempted suicide (Hawton and van Heeringen, 2009), improving the prediction of future self-harm in individuals who previously attempted suicide is particularly relevant. Of course, this individual approach based on the prediction of self-harm repetition adds up to other recognized global interventions, which may also be interesting for individuals who never attempted before, e.g. access restriction to lethal means or improved recognition and treatment of depression (Mann et al., 2005).

Examining repetition in terms of self-harm can be understood in two main ways: repeating self-harm over a period of follow-up (either retrospectively or prospectively), and comparing individuals with a single episode of self-harm and those with multiple self-harm at one specific time point (which is by nature retrospective).

1.3 Can we use neurocognition to predict repetition of self-harm?

Self-harm is likely to be best understood as a complex interaction between individual factors (such as personality traits), and variable social and health events (such as employment, interpersonal, legal or financial stress, current mental and physical state), moderated by socio-demographic variables (age, sex, cultural factors) (Hawton and van Heeringen, 2009). The identification of the individual factors increasing the risk of suicidal acts in a stressful situation is the aim of numerous studies worldwide. For instance, it may allow the identification of individuals at higher suicide risk among depressed patients.

Recently, there has been increasing exploration of potential brain structural and functional abnormalities, and the associated deficits in cognitive functions (globally known as neurocognitive correlates or factors), in patients who have a history of self-harm (Richard-Devantoy et al., 2014a; van Heeringen et al., 2014). These factors have the advantage of potentially acting as objective markers, overcoming the biases present with self-reports, for instance reports of past, current or future suicidal intent (Glenn and Nock, 2014). Recent systematic reviews into the brain structural and functional abnormalities associated with self-harm suggest that the main regions involved include the orbitofrontal cortex (OFC), ventromedial prefrontal cortex (VMPFC), dorsolateral prefrontal cortex (DLPFC), and anterior cingulate cortex (ACC), indicating potentially impaired functioning of the prefrontal network (Cox Lippard et al., 2014; Jollant, 2016; Jollant et al., 2011; Van Heeringen et al., 2011; van Heeringen et al., 2014; van Heeringen and Mann, 2014), in addition to other regions including the parietal cortex, some subcortical nuclei and possibly the cerebellum (Gifuni et al., 2016; Jollant et al., 2008a; Richard-Devantoy et al., 2016a).

Dysfunctions of these brain areas are thought to underlie several cognitive deficits observed in individuals with a history of self-harm (mainly middle-aged adults and more rarely in adolescents and elderly). The factors identified include risky decision-making (Clark et al., 2011; Jollant et al., 2005; Jollant et al., 2010; Oldershaw et al., 2009; Richard-Devantoy et al., 2014a), weak problem solving abilities (D'Zurilla et al., 1998; Pollock and Williams, 2004), deficient cognitive inhibition and high sensitivity to interference (Keilp et al., 2014; Richard-Devantoy et al., 2014a; Richard-Devantoy et al., 2012), memory problems (Richard-Devantoy et al., 2015), and altered implicit processing and explicit recognition of emotional signals (Jollant et al., 2008b; Pan et al., 2013; Richard-Devantoy et al., 2013a). While these observations may be important to understand the mechanisms underlying complex behaviours, it is uncertain if we can use assessment of these factors in an individual to predict the risk of future self-harm. Therefore, in this systematic review, we aimed to assess the presence and extent of any associations between neurocognitive factor assessments and repetition of self-harm.

Previous systematic reviews on repetition of self-harm have: (i) focussed only on certain forms of self-harm (Fliege et al., 2009); (ii) included little or no data on potential neurocognitive factors (Mendez-Bustos et al., 2013); (iii) focussed only on psychometric tools in hospital (Randall et al., 2011); (iv) focussed only on hospital admissions (Larkin et al., 2014). As far as we are aware, there is no previous systematic review of the major neurocognitive factors and repetition of self-harm, inclusive of all forms of self-harm and all settings.

2. Methods

We used the Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA) for guidance regarding reporting of search, extraction and synthesis of results (Liberati et al., 2009). In accordance with these guidelines, the protocol for the systematic review was registered on PROSPERO (http://www.crd.york.ac.uk/PROSPERO/), registration number: CRD42015017793.

2.1 Eligibility criteria

Articles were assessed for inclusion according to the following criteria: (i) published in a peer-reviewed journal in English; (ii) investigated neurocognitive functions with tasks or scales; (iii) investigated repetition of self-harm; and (iv) involved adolescent, adult or elderly people. Repetition of self-harm was defined as either (i) multiple episodes of self-harm ("multiple") versus first episode of self-harm ("single") or (ii) current suicidal ideation or self-harm on background of past self-harm ("repeaters") versus no current suicidal ideation or recent self-harm on background of past self-harm ("non-repeaters"). Details of inclusion and exclusion criteria are available in supplementary material.

2.2 Information sources

Relevant studies were identified using tailored electronic searches with MeSH and textword terms for the following databases:

- Medline
- Embase
- PsycINFO

- CINAHL
- The Cochrane Library
- Web of Science

To maximise the comprehensive nature of information collection, reference lists of appropriate review articles and a book chapter (Arensman et al., 2011) were also screened and a hand search of recent (January 2014 to February 2015) editions of appropriate journals was performed (British Journal of Psychiatry, Suicide and Life-Threatening Behavior).

2.3 Search strategy

Databases were searched from inception to March 2015. The following terms were used to search all databases: repeat, persist, predict, repetition, self-harm, deliberate self-harm, suicidal behaviour, self-mutilation, self-injury, decision-making, problem solving, aggression, impulsivity, arousal, emotion, facial expression, affect, amygdala, orbitofrontal cortex, anterior cingulate cortex, and dorsolateral prefrontal cortex. All variations of spelling of text terms were used (e.g. self-harm and self harm). Search terms were truncated as appropriate and MeSH or equivalents were used to maximise the comprehensive nature of the searches. Search strategies tailored to each database were checked with a skilled medical librarian. There was no restriction in terms of date of publication. However, the search was restricted to English language publications. The Medline search strategy, and results for each database search, can be found in the appendix.

2.4 Study selection

The first phase of selection involved screening of titles and abstracts against inclusion criteria to assess eligibility. Each reference was screened by two of four authors (AdeC, BP, KB, KJ) using reference software (EndNote). In the second phase of selection, the full-text of studies determined to be eligible in phase one was examined against inclusion criteria by two of the following authors (AdeC, KR, MB, BP, KB, KJ, EL, FJ). Any disagreements were resolved by discussion and the use of a third author.

2.5 Data extraction

Data were extracted from studies meeting inclusion criteria using a pre-specified database as recommended by the Cochrane Handbook (Higgins & Green, 2011). Data extracted from each study included:

- General study characteristics (including study type, duration of follow-up if appropriate)
- Participant characteristics (including total and individual group numbers, mean age, gender ratio, country, any diagnosis specified at recruitment, setting)
- Details of exposure: neurocognitive factor (including which assessed, details of assessment methods)
- Details of outcome: self-harm (including how self-harm assessed / definition of self-harm used, form of repetition)
- Study results (including attrition, percentage of repetition found in study, significant findings and statistical results where given)

2.6 Risk of bias assessment

We appraised risk of bias using the Newcastle-Ottawa Scale (NOS) for longitudinal cohort and case-control studies as recommended by the Cochrane Handbook

(Higgins and Green, 2011), and used the STROBE Collaboration (von Elm et al., 2007) individual component checklists to appraise studies of any type. We determined that a study was at moderate to high-risk of bias if there were at least seven missing or unclear items (not including not applicable items) out of a possible 34 items on the STROBE, and five or less out of a possible eight stars on the NOS where this was also applicable. Scales are available in supplementary material.

2.7 Analysis

Included studies were reviewed and critically appraised, and data synthesised. Study findings were categorised on the basis of the assessed neurocognitive factor. Groupings for analysis were as follows: (i) cognitive control (including attention, inhibition, interference and working memory); ii) value-based decision-making and related processes (delay discounting, decision-making); iii) problem solving; iv) memory processing (short and long-term and autobiographical); v) emotional-processing; and vi) neuroimaging. These groupings were determined by neurocognitive factor categorisation in the literature (Dixon and Christoff, 2014; Glascher et al., 2012; Richard-Devantoy et al., 2013b) and the expert opinion of the authors. The analysis group, cognitive control, was formed particularly in reference to the previous literature relating to deficient cognitive inhibition and high sensitivity to interference (Keilp et al., 2014; Richard-Devantoy et al., 2014a; Richard-Devantoy et al., 2012). For the group, we included all studies meeting inclusion criteria and where the neurocognitive measure related to attention, inhibition, interference and / or working memory.

Within each neurocognitive factor, study findings were subdivided into studies addressing objective 1 (retrospective: “multiple vs. single” or “repeaters vs. non-repeaters”) or objective 2 (prospective: “repeaters vs. repeaters”). *A priori*, it was expected that data synthesis would be narrative as the search would result in included studies with heterogeneity in terms of study type, participants and methods.

3. Results

3.1 Study selection

6990 records were identified from database searches after de-duplication and 35 records from hand-searching of reference lists, relevant journal searches and expert advice. 6857 records were excluded following appraisal of title and abstract. 168 full-text articles were assessed for eligibility. 153 full-text articles were excluded, with reasons for each given in the PRISMA diagram (figure 1). The majority of studies were excluded because they did not examine repetition of self-harm. Two articles were excluded because of a lack of clarity about inclusion after we had attempted to contact the study authors. 15 unique studies met inclusion criteria. Full details are presented in the PRISMA flow diagram (figure 1).

Figure 1 about here

3.2 Included study characteristics

15 unique studies were included in the analysis. 10 were longitudinal studies, 2 were case-control in design and 3 were cross-sectional. Findings were analysed in specific groupings according to neurocognitive factor(s) under investigation. Details of all risk of bias assessments are included in supplementary material.

Table 1 (Characteristics of included studies) about here

3.3 Cognitive control

Seven studies assessed cognitive control in terms of predicting repetition of self-harm. Study characteristics are given in table 1, and a summary table with study findings is given in table 2.

3.3.1 Study design

Four studies involved longitudinal designs (Cha et al., 2010; Larkin et al., 2013; Nock et al., 2010; Pluck et al., 2013), one study used a case-control design (Dougherty et al., 2004) and two studies were cross-sectional (Mathias et al., 2011; Swann et al., 2005).

3.3.2 Participants

Study sample sizes varied from 29 to 157 participants. All studies were conducted in Western countries (United States, UK, Ireland and Germany). Two studies included participants with a single mental illness diagnosis at baseline (bipolar disorder (Swann et al., 2005), and schizophrenia (Pluck et al., 2013)), whereas other studies did not restrict participants in this manner. One study included only adolescents (Mathias et al., 2011) with all other studies including just adults. In terms of patient recruitment, one study recruited participants from the community only (Dougherty et al., 2004), three studies recruited patients from emergency departments (Cha et al., 2010; Larkin et al., 2013; Nock et al., 2010), one study recruited community patients / psychiatric outpatients and inpatients (Pluck et al., 2013), and the remainder recruited only psychiatric inpatients.

3.3.3 Exposure

Cognitive control was assessed by:

- Emotional Stroop – modified (Cha et al., 2010; Larkin et al., 2013)
- Go/No-Go test (Mathias et al., 2011; Pluck et al., 2013)
- Continuous Performance Test – all versions (CPT) (Dougherty et al., 2004; Pluck et al., 2013; Swann et al., 2005)
- Trail Making Test (TMT) (Pluck et al., 2013)
- Implicit Associations Test (IAT) (Nock et al., 2010)

3.3.4 Outcome

Of the four longitudinal studies, three assessed repetition of self-harm or suicide attempts over follow-up (Cha et al., 2010; Larkin et al., 2013; Nock et al., 2010; Pluck et al., 2013). Therefore, all four of these studies provided prospective data for objective 2 (“repeaters vs. non-repeaters” or “current + past vs. past only). The case-control and cross-sectional studies assessed multiple versus single suicide attempts in participants (Dougherty et al., 2004; Mathias et al., 2011; Swann et al., 2005), therefore providing data for objective 1 (“multiple vs. single”).

3.3.5 Findings

A summary of results for each study can be seen in table 2.

Table 2 (Cognitive control: summary and study findings) about here

Findings were mixed in terms of facets of cognitive control predicting repetition of self-harm.

3.3.5.1 Retrospective (multiple versus single)

One study showed significant associations. Dougherty and colleagues found a strong association between cognitive control and repetition of self-harm (Dougherty et al., 2004): scores on a modified version of the CPT predicted multiple suicide attempt group versus single suicide attempt group on both the immediate memory test ($p=0.011$) and delayed memory test conditions ($p= 0.012$).

The other studies found no association (Mathias et al., 2011;; Swann et al., 2005). In Mathias et al., there were no group differences on the Go-Stop task (Mathias et al., 2011). Swann et al. discovered no association between sustained attention measured with the CPT and repetition of self-harm in secondary analyses (Swann et al., 2005), but no statistics were reported.

3.3.5.2 Prospective (repeaters versus non-repeaters)

Two studies showed significant associations. In Nock et al.'s study, death-related words predicted occurrence of future suicide attempts above and beyond clinical predictors ($p<0.05$), and participants with a stronger association on the IAT between death/suicide and self were significantly more likely to make a suicide attempt after leaving the emergency department (31.8%) over a six month period than were those with a stronger association between life and self (10.1%) ($p<0.05$). One subdomain of Cha et al., yielded a borderline association between attentional bias toward suicide-related words measured with an Emotional Stroop task and repetition of self-harm: suicide-related words were just predictive of repetition of suicidal attempts over six month follow-up (OR 1.02 (95% CI 1.00-1.03)) (Cha et al., 2010). Two studies found no association. In Larkin et al., a modified Emotional Stroop task found that neither low stimulation ($p=0.36$) or high stimulation ($p=0.79$) predicted repeaters compared to non-repeaters, and Pluck et al. showed no association in patients with schizophrenia between sustained and selective attention according to the CPT and response inhibition as measured by a Go/No-Go task and repetition of self-harm in secondary analyses, but no statistics were reported.

3.3.6 Risk of bias assessment

Three studies assessing cognitive control and repetition of self-harm were at a moderate to high-risk of bias according to both the NOS and STROBE where appropriate (Dougherty et al., 2004) and STROBE only for a cross-sectional study (Mathias et al., 2011; Swann et al., 2005). Therefore, there needs to be caution in

interpreting the findings of these individual studies. Other studies were not at high-risk.

3.4 Value-based decision-making

Two studies studied whether value-based decision-making is associated with repetition of self-harm in adolescents. Of note, none assessed decision-making in a social context (e.g. ultimatum game, trust game, prisoner's dilemma). Study characteristics are found in table 1, with an overview and study findings in table 3.

3.4.1 Study design

Oldershaw and colleagues' 2009 study was case-control in design, whereas Mathias et al. 2011 was cross-sectional.

3.4.2 Participants

Mathias and colleagues' study was small, involving 59 participants, and there was no diagnosis specified at recruitment (Mathias et al., 2011). The sample in the Oldershaw and colleagues study (Oldershaw et al., 2009) was twice the size and all participants had depressive disorder. Both only included adolescent participants.

3.4.3 Exposure

Oldershaw et al. assessed decision-making using the Iowa Gambling Task (IGT) (Oldershaw et al., 2009), whereas Mathias et al. assessed decision-making using the Two Choice paradigm (Mathias et al., 2011).

3.4.4 Outcome

In the studies, Oldershaw et al. (Oldershaw et al., 2009) assessed broader self-harm, whereas Mathias et al. assessed all self-harm and suicide attempts (Mathias et al., 2011). However, the studies assessed different forms of repetition. Oldershaw

et al. (Oldershaw et al., 2009) compared presence or absence of current self-harm in those with only a history of self-harm (objective 2 - retrospective), whereas Mathias et al. assessed multiple vs single suicide attempts (objective 1).

3.4.5 Findings

A summary of results for each study can be seen in table 3.

Table 3 (Value-based decision-making: summary and study findings) about here

Both studies found associations between impaired decision-making and repetition of self-harm (Mathias et al., 2011; Oldershaw et al., 2009).

3.4.5.1 Retrospective (single versus multiple)

In Mathias and colleagues' study, the Two-Choice task results were significantly different between participants with multiple and single suicide attempts ($p<0.001$) (Mathias et al., 2011).

3.4.5.2 Retrospective (repeaters versus non-repeaters)

In Oldershaw, those continuing to self-harm were significantly more likely to have lower scores on the IGT and were less likely to improve their scores over the task than those not continuing to self-harm (Oldershaw et al., 2009). However, interestingly, mean number of total DSH episodes was higher in the past self-harm only group than the current self-harm group.

3.4.6 Risk of bias assessment

One of the two studies was at moderate to high-risk of bias according to the STROBE checklist (Mathias et al., 2011). Therefore, the results of this study should be viewed with caution. The other study was not at high-risk of bias.

3.5 Problem solving

Eight studies used cognitive tasks to measure associations between problem solving and repetition of self-harm. Study characteristics are found in table 1, with an overview and study findings in table 4.

3.5.1 Study design

One study was case-control in design (Oldershaw et al., 2009). The seven remaining studies were longitudinal.

3.5.2 Participants

All studies were conducted in Western countries: three in the United States (Goldston et al., 2001; Hughes and Neimeyer, 1993; Kehrer and Linehan, 1996), two in the UK (Hawton et al., 1999; Oldershaw et al., 2009), two in Ireland (Larkin et al., 2013; McAuliffe et al., 2008) and one in Norway (Dieserud et al., 2003). Three studies included only adolescents (Goldston et al., 2001; Hawton et al., 1999; Oldershaw et al., 2009) with the remainder adults. Two studies specified diagnosis at recruitment: Kehrer et al. (Kehrer and Linehan, 1996) involved adults with borderline personality disorder, and Oldershaw et al. (Oldershaw et al., 2009) recruited adolescents with depression. The other six studies did not restrict by diagnosis. Included studies also varied in size: several studies recruited 50 or fewer participants (Dieserud et al., 2003; Hawton et al., 1999; Kehrer and Linehan, 1996; Larkin et al., 2013), whereas Goldston and colleagues study involved over 200 participants (Goldston et al., 2001). However, unlike studies assessing cognitive control, there were no large cohort studies with more than 1000 participants.

3.5.3 Exposure

Two different cognitive tests were used to assess problem solving. Each measure and the corresponding studies involved is given below.

- Means Ends Problem solving Procedure (MEPS) or modifications of this: (Dieserud et al., 2003; Goldston et al., 2001; Hawton et al., 1999; Hughes and Neimeyer, 1993; Kehrer and Linehan, 1996; Larkin et al., 2013; Oldershaw et al., 2009)
- Optional Thinking Test (OTT): (McAuliffe et al., 2008)

3.5.4 Outcome

The studies included participants with different forms of self-harm. Three studies included those with suicide attempts (Dieserud et al., 2003; Goldston et al., 2001; Larkin et al., 2013), three studies parasuicide (Hughes and Neimeyer, 1993; Kehrer and Linehan, 1996; McAuliffe et al., 2008), and two studies self-harm (Hawton et al., 1999; Oldershaw et al., 2009). However, two studies did not define how they interpreted the specific term they were using (Hughes and Neimeyer, 1993; Larkin et al., 2013). Hawton and colleagues study only included those who had a self-harm episode involving self-poisoning (Hawton et al., 1999).

The studies assessed different forms of repetition. Of the longitudinal studies, four studies assessed repeaters compared to non-repeaters at follow-up only (Dieserud et al., 2003; Hughes and Neimeyer, 1993; Kehrer and Linehan, 1996; Larkin et al., 2013), (objective 2 - prospective) whereas three studies assessed repetition at baseline and follow-up (Goldston et al., 2001; Hawton et al., 1999; McAuliffe et al., 2008) (objective 1 and 2 - prospective). Oldershaw et al.'s case control study assessed those with continuing self-harm compared to past self-harm only (Oldershaw et al., 2009) (objective 2 – retrospective).

In terms of the pre-determined objectives, the three studies assessing repetition of self-harm at baseline and follow-up provided evidence for objectives 1 and 2 (Goldston et al., 2001; Hawton et al., 1999; McAuliffe et al., 2008). The other five studies provided evidence for objective 2 only.

3.5.5 Findings

A summary of the results can be seen in table 4.

Table 4 (Problem solving: summary and study findings) about here

3.5.5.1.1 Retrospective (multiple versus single)

One study showed an association between problem solving using the OTT and repetition of self-harm (McAuliffe *et al.*., 2008). Low scores on both subdomains of relevant options and relevancy ratio predicted multiple self-harm versus single self-harm at baseline (p=0.011, p=0.014). Furthermore, repetition at baseline and follow-up was predicted by low scores on the subdomain of relevancy ratio (p=0.012).

The two other studies did not find associations between self-harm repetition and problem solving. Goldston et al. 2001 found that there were no significant associations between MEPS scores and repetition of self-harm but statistics were not given; Hawton found no associations between problem solving using the MEPS and either multiple versus single self-harm (though no statistics were given) or repetition at follow up (where total and effectiveness subdomains were significant on initial analyses ($p<0.05$ for both) but were non-significant once they controlled for scores on the Beck Depression Inventory);

3.5.5.1.2 Retrospective (repeaters versus non-repeaters)

Oldershaw et al. 2009 demonstrated no association between problem solving on the MEPS and repetition of self-harm (continuing self-harm versus past self-harm only), but no statistics were reported.

3.5.5.2. Prospective (repeaters versus non-repeaters)

For two studies (Hughes & Neimeyer, 1993; Kehrer & Linehan, 1996), only certain subdomains of the problem solving measure involved were associated with repetition of self-harm: for Hughes et al., using a modified MEPS, the subdomain assessing alternative problem solving showed an effect of group between current and non-current self-harm on a background of self-harm, but no statistics were given; for Kehrer et al,, inappropriate means scores on the MEPS at 4 and 8 months ($p<0.001$ and $p<0.1$) and combined MEPS scores at pre-treatment, 4 months and 8 months for inappropriate means and passive means to ends ($p<0.0001$) predicted current self-harm versus non-current self-harm.

The other two studies found no association between any subdomains of cognitive problem solving on the MEPS and repetition of self-harm: Larkin et al. found that overall MEPS score was not predictive of repeat self-harm ($p=0.76$); Dieserud et al. 2003 similarly found that there were no significant associations between MEPS scores and repetition of self-harm but statistics were not given

3.5.6 Risk of bias assessment

One study where at least one subdomain of impaired problem solving and repetition of self-harm were found to be associated was at moderate to high-risk of bias according to the NOS assessment and STROBE checklist (Hughes and Neimeyer, 1993). Therefore, we may need to be cautious when placing weight on the study

findings. Other studies were not at a high-risk of bias according to all results available.

3.6 Memory

Two studies analysed facets of memory with repetition of self-harm. Study characteristics are found in table 1, with an overview and study findings in table 5.

3.6.1 Study design

One study was longitudinal in design (Larkin et al., 2013) and one study was cross-sectional (Rasmussen et al., 2008).

3.6.2 Participants

All studies were conducted in Western countries: one in the UK (Rasmussen et al., 2008), and one in Ireland (Larkin et al., 2013). All studies involved adults. The studies were both small: Rasmussen et al. involved 40 participants, and Larkin et al. involved 29 participants.

3.6.3 Exposure

Both studies used tasks assessing autobiographical memory.

3.6.4 Outcome

The studies assessed different forms of self-harm. One study assessed suicide attempts (Larkin et al., 2013), and one study assessed broader self-harm (Rasmussen et al., 2008) but neither defined their understanding of the term used.

The studies assessed different forms of repetition. Larkin et al. assessed repeaters compared to non-repeaters at follow-up only (objective 2 – prospective) (Larkin et al.,

2013). Rasmussen et al. assessed multiple episodes of self-harm versus a single episode (objective 1) (Rasmussen et al., 2008).

3.6.5 Findings

Details of results can be seen in table 5.

Table 5 (Memory processing: summary and study findings) about here

3.6.5.1 Retrospective (multiple versus single)

Rasmussen et al. found an association between a particular impairment in autobiographical memory (recall of positive memories ($p < 0.05$), but not negative memories (non-significant, but no statistic given) and repetition of self-harm (Rasmussen et al., 2008).

3.5.6.2. Prospective (repeaters versus non-repeaters)

Larkin et al. 2013 found that total or subdomain scores on an autobiographical memory task did not demonstrate group effects in terms of repeaters vs. non-repeaters of self-harm: total scores ($p=0.17$), positive memories ($p=0.16$), negative memories ($p=0.51$).

3.6.6 Risk of bias assessment

Neither of the studies was found to be at high risk of bias.

4. Discussion

4.1 Overview of neurocognitive results

There were 15 studies included in this review. Seven studies assessed cognitive control (including attention, interference and response inhibition), two studies value-based decision-making, eight studies problem solving, and two studies autobiographical memory. There were no data available for other neurocognitive factors. Only one quarter (n=4) of studies involved adolescents. Two studies assessed participants with diagnosed affective disorders at baseline, and only one each with personality disorder and schizophrenia. Overall, the results were inconsistent for cognitive control, although one longitudinal study suggests a potential predictive value of the IAT in terms of repetition. Results were also inconsistent for autobiographical memory, although there were too few and heterogeneous studies to draw conclusions from this. There were two cross-sectional studies with data for impaired decision-making in adolescents and both were predictive of repetition of self-harm. The majority of problem solving studies did not demonstrate any association between problem solving and repetition of self-harm. There were no data available for other facets of memory (working memory, long-term memory), or for strategic decision-making in a social context. There were also no data for emotional-processing or imaging studies.

4.2 Studies excluded from the review

153 studies were excluded following review of the full text. A summary of reasons for exclusion is given in the PRISMA diagram (figure 1). Many studies were excluded because data collected in terms of neurocognition and repetition of self-harm had not been analysed together. This is an important point for the research community in general to consider when planning future analyses of similar studies.

One excluded study was a conference abstract where a detailed publication of the data was in submission according to the study authors (Blumberg, 2014). As it is likely the full publication would meet inclusion criteria, the characteristics of this study are presented in the appendix.

4.3 How current findings relate to the literature

4.3.1 Cognitive control

Cognitive control is a set of flexible and adaptive brain processes, which come into play when we engage in intentional actions, as opposed to unintentional and inflexible automatic brain processes (Egner and Hirsch, 2005). Cognitive tasks designed to explore an individual's cognitive control aim to simultaneously activate automatic and conscious responses to the same stimulus, which depending on the situation may give rise to a conflict in that individual (Cona et al., 2016; Lu and Proctor, 1995). A classical issue in neuropsychology is that most tasks activate multiple cognitive functions (e.g. Go/No-Go and attention, working memory and response inhibition (Criaud and Boulinguez, 2013)).

In this review, there was inconsistency for cognitive control tasks in terms of associations with repetition. This was particularly true for the related tasks, the CPT

and the Emotional Stroop, where two or more studies using the same task provided opposing findings in terms of ability of task results to predict repetition. However, one study (Nock et al.) found that death-related words predicted occurrence of future suicide attempts above and beyond clinical predictors ($p<0.05$), indicating that this task is worthy of further research.

This inconsistency is also reflected in the literature on self-harm in general: in a meta-analysis of nine studies, performances on the cognitive Stroop task were found to differentiate between suicide attempters and patient controls (Richard-Devantoy et al., 2014a), but also in this meta-analysis, the CPT did not show clear differences between these patient groups. A separate recent meta-analysis restricted to the emotional version of the Stroop task also suggested a significant bias toward suicide-related words in suicide attempters compared to patient controls (Richard-Devantoy et al., 2016b), although this effect was small and may be dependent on the depressive state more than vulnerability traits.

Both included studies in our review using Go-Stop tasks failed to find any association with repetition, suggesting that this task may show more consistency of results. The lack of association between the classical Go/No-Go and repetition of self-harm is in line with recent neuroimaging findings showing that brain responses during this task did not discriminate between attempters and non-attempters (Richard-Devantoy et al., 2016a). Nonetheless, outwith of this review, Westheide and colleagues provide evidence that there may an association between performance on a Go-Stop task and prediction of future suicidal ideation in participants with previous self-harm (Westheide et al., 2008).

In terms of frontal functioning tasks, the one included study (Pluck) failed to find any association between repetition and the TMT. Westheide and colleagues also showed no association between delayed alternation and impairments in selective attention with repetition (Westheide et al., 2008). However, Miranda et al. found that impairments in cognitive flexibility on the Wisconsin Card Sorting Test did predict future suicidal ideation on a background of previous self-harm (Miranda et al., 2012), and Fikke et al. found an association between impaired frontal functioning and self-harm not related to specific diagnosis using set-shifting tasks (Fikke et al., 2011).

In summary, at this point in time, we are unable to clarify if, and which particular aspects, of cognitive control may be relevant in terms of associations with repetition of self-harm. However, specific tasks may be important.

4.3.2 Problem solving

There were a moderate number of studies assessing problem solving and repetition of self-harm (n=8). The majority of studies did not demonstrate an association between cognitive assessments of problem solving and repetition of self-harm; only McAuliffe and colleagues' 2008 study found such an association (McAuliffe et al., 2008), which interestingly used a different measure (OTT) to all the other included studies (MEPS).

Definition of problem solving as a neurocognitive factor is particularly important, and open to a certain level of interpretation when examining the existing literature in self-harm: problem solving may be used by study authors to describe what they later detail as coping styles or strategies, or resilience. McAuliffe used the Utrecht Coping List to assess "problem solving" in her 2006 study, which determined that certain subdomains were associated with repetition of self-harm (McAuliffe et al., 2006).

Furthermore, some authors suggest that problem solving deficits in self-harm may be linked with problems with autobiographical memory (Pollock and Williams, 2001; van Heeringen, 2003), and so the two constructs may need to be considered together in research.

Despite conflicting evidence surrounding problem solving and repetition of self-harm, the majority of recent studies investigating problem solving and self-harm are trials (or protocols of trials) of problem solving interventions to reduce self-harm repetition (Collinson et al., 2014; Hatcher et al., 2015; Husain et al., 2011; McAuliffe et al., 2014); but few show particular promise as yet. As the underlying research base may still be equivocal, it potentially throws into question whether we are running ahead of the evidence by trialling interventions when it is not clear to what extent, and potentially what component of, impaired problem solving may be associated with repetition.

4.3.3 Value-based decision-making

There were only two studies assessing value-based decision-making in the current review, but both demonstrated associations between impaired decision-making and repetition of self-harm in adolescents, although they varied in baseline mental health status (Mathias et al., 2011; Oldershaw et al., 2009). Value-based decision-making involves the use of cognitive processes required to balance rewards, the expected value of such outcomes, as well as the delays and efforts involved, and feedback received (Dixon and Christoff, 2014). The core regions associated with such processes have been identified as the ventromedial prefrontal cortex (VMPFC), orbitofrontal cortex (OFC), and cingulate cortex, as well as the ventral striatum and amygdala (Dixon and Christoff, 2014),

Although outside of our inclusion criteria, Malloy-Diniz and colleagues found further evidence to support a link between repeat self-harm and decision-making: there was a significant negative correlation between the number of suicide attempts and decision-making results (as measured with the IGT) (Malloy-Diniz et al., 2009). Studies assessing general self-harm behaviour and decision-making also provide support. A recent meta-analysis of neurocognitive factors and general suicidal behaviour found that, over nine studies, IGT scores were significantly lower in 299 suicide attempters than 281 patient controls with a moderate effect size (g=-0.47, 95% confidence intervals -0.65 to -0.29) as well as 250 suicide attempters versus 350 healthy controls (Richard-Devantoy et al., 2014a). Furthermore, adolescents who previously self-harmed but are no longer engaging in this behaviour appear to have normal decision-making abilities (Oldershaw et al., 2009), indicating that perhaps deficits in decision-making are specific to current self-harm. However, Jollant authored two studies that were unable to provide supportive evidence, but which did not meet inclusion criteria. In his 2005 non-imaging study, there was no significant correlation in secondary analysis between the number of suicide attempts and performance on the IGT (Jollant et al., 2005). There was also no correlation between adults who showed risky decision-making and activation in the lateral orbitofrontal cortex, and the number of previous self-harm episodes in a later fMRI study (Jollant et al., 2010).

Therefore, considering the supportive data so far in terms of self-harm, and for repetition, decision-making could be a clinically important factor for self-harm risk prognostication and therapy, and definitely merits future research attention.

4.4.4 Memory processing

There were too few studies (n=2), both limited to autobiographical memory, to draw any firm conclusions from the inconsistency of results.

There is some cognitive plausibility for this factor to be involved with self-harm behaviour: impaired autobiographical memory storage and recall might prevent an individual from using these memories appropriately to protect themselves from any painful future consequences (Liu et al., 2013) and from using these memories to guide problem solving (van Heeringen, 2003).

Other studies, which did not meet criteria for inclusion in the current review, found associations between impairments in memory (especially autobiographical memory) and repetition of self-harm (Richard-Devantoy et al., 2015). Sinclair found that low memory specificity mediated the association between childhood sexual abuse and “recent” self-harm episodes (Sinclair et al., 2007). However, it was not able to be included because it classified “recent self-harm” as occurring within the last year, which was an exclusion criteria for the current review. Larkin and colleagues’ systematic review of prospective hospital studies found that a few studies assessed autobiographical memory and overall there was a small association with repetition of self-harm (Larkin et al., 2014). There may also be other important aspects of memory: Martinez-Aran determined that impairments of verbal memory (on the California Verbal Learning Test) were correlated with the number of suicide attempts in secondary analyses (Martinez-Aran et al., 2004).

In summary, no conclusions can be drawn from this review due to limited evidence. However, the included studies put in the context of other evidence suggest that

further research is merited to determine if associations do exist, and to what extent impairments in different memory domains may predict repetition of self-harm.

4.4.5 Emotional-processing (and the close relation with imaging studies)

There were no data for emotional-processing in this review. However, as previously mentioned, we await further report of findings from a conference abstract which used imaging methods (structural MRI, fMRI, diffusion tensor imaging) and an emotional-processing (faces) task alongside other tasks (Blumberg, 2014). The study was longitudinal involving adolescents with suicide attempts and either bipolar disorder or depressive disorder, and matched healthy controls.

Work on emotional-processing usually requires use of imaging methods. Jollant and colleagues performed a seminal emotional-processing study, demonstrating that in remitted patients with self-harm history compared to patient controls there was increased activation in the right OFC to angry faces and in the right anterior cingulate cortex (ACC) to mild happy versus neutral faces (Jollant et al., 2008b). In this study, the number of previous self-harm episodes was recorded, but this was not analysed alongside the emotional processing data. Pan et al. partly replicated this important work in adolescents: they also found activation level changes in the ACC and related brain areas on happy and angry versus neutral faces (Pan et al., 2013) in adolescents with suicidal attempts versus depressed controls. Therefore, emotional processing appears to be an important facet of neurocognition in terms of self-harm, and thus it deserves further investigation into its relevance for predicting repetition.

4.4.6 Other important findings from imaging studies

Imaging studies in neurocognition and self-harm would allow us to connect structural brain abnormalities with functional changes, and so understand the underlying

cognitive mechanisms. Van Heeringen and colleagues published a recent systematic review and meta-analysis of structural and functional MRI studies examining general suicidal behaviour (van Heeringen et al., 2014), identifying activation foci from 12 studies including 213 suicide attempters with mental illness and 262 psychiatric controls. In those with suicidal history, compared to without, there was an increased activation during emotional tasks (such as exposure to emotionally-charged faces) in the rostral ACC, and decreased activation during non-emotional cognitive tasks (such as the IGT (decision-making), or the Go/No-go task (cognitive control)) in the dorsal ACC (van Heeringen et al., 2014). Previous studies have demonstrated decreased grey matter in the OFC, ACC, and prefrontal cortex (PFC) associated with suicide attempts (Benedetti et al., 2011; Monkul et al., 2007), and volume changes of the right amygdala (Monkul et al., 2007). These structural abnormalities may impair the functioning of the amygdalo-orbitofrontal-cingulate network, thereby preventing the amygdala from inhibiting the OFC and PFC, and the OFC from inhibiting the ACC appropriately (de Cates and Broome, 2016). The neurocognitive factors in the current review are thought to be located or connected to these brain regions and network.

4.4 Strengths and limitations of this systematic review

There were several strengths of this current review, including a comprehensive data search, duplication of processes with good agreement, and an assessment of risk of bias for all included studies. Due to the high level of heterogeneity in included studies, even after dividing into groupings based on neurocognitive factor, we avoided an inappropriate meta-analysis (Higgins and Green, 2011).

Unfortunately, non-English studies were excluded, and most studies were conducted in adults, in Western countries, and using participants with no specific diagnosis. This therefore limits the generalisability of review findings to other populations.

Self-harm is a global problem, with approximately one million deaths per year around the world (WHO, 2015). Moreover, differences in cognitive functions have been shown between different cultural groups (Han and Northoff, 2009). A hypothesis that culture may modify the relationship between cognition and suicide risk will need to be specifically tested. The paucity of data in adolescents is a common problem, especially present in self-harm research, due to extra safeguards in terms of ethical approval, recruitment and consent (Barzilay and Apter, 2014; Hawton et al., 2012), and when assessing neurocognitive factors (Gorlyn, 2005). Moreover, no study directly compared age groups, preventing us to examine potential differences in the link between cognitive functioning and repetition of self-harm according to developmental and aging stages. Self-harm and the relationship with diagnosis is a complicated issue. The Research Domain Criteria approach of the NIMH does suggests that we should be focussing on trans-diagnostic processes (Walter, 2013). Nonetheless, the presence of a specific illness may have some relevance: Hawton and colleagues have shown the potential importance of the diagnosis of depression in particular in self-harm research (Hawton et al., 2013; Hawton et al., 1999), although the vast majority of those with depression do not attempt suicide (Chen and Dilsaver, 1996). Furthermore, and perhaps surprisingly, some studies in patients with schizophrenia showed cognitive deficits to be more pronounced in those without self-harm history as opposed to those with self-harm (Richard-Devantoy et al., 2014b). Therefore, it seems likely that self-harm needs to be understood in the context of any mental illness present, but not be defined by its presence or absence. In our review,

only one included study exclusively recruited patients with depression (Oldershaw et al., 2009), and so it was not possible to assess the extent of depression on trait-dependent neurocognitive vulnerability.

Another issue with research examining repetition of self-harm is that self-harm and particularly suicide are rare events. To be comprehensive and maximise data available for analysis, all types of self-harm were included. Therefore, studies assessing non-suicidal self-injury (NSSI) / self-injurious behaviour (SIB) were included as a type of self-harm at baseline and at follow-up. Some may argue that NSSI is not related to suicide attempts, especially in the United States where NSSI has been segregated from “suicidal behaviour syndrome” in the new DSM-5 (APA, 2015). However, the majority of the evidence indicates that any form of self-harm, regardless of intent, increases the risk of future self-harm and suicide (Brent, 2011; Groschwitz et al., 2015; Owens et al., 2002; Wilkinson et al., 2011).

Self-harm in all settings (hospital and community) and using all methods (self-cutting, overdose, hanging etc.) were included in the current review for comprehensiveness, and analysed together. It is difficult to determine if there is a difference between community and hospital presentations of self-harm due to a lack of direct comparison studies, and excluding community self-harm risks under-representing repetition in particular. We therefore noted the setting for each study and made this clear in the study characteristics tables for each neurocognitive factor. Some have argued that psychological underpinning of individuals with different methods may be different: self-cutters may be undertaking this behaviour to release tension, whereas those who overdose for example may be more motivated by thoughts of death (Rodham et al., 2004). However, recent cohort analysis indicates that many individuals switch self-harm methods in subsequent episodes, and so division of participants by

methods alone for prediction of repetition may not be appropriate (Owens et al., 2015).

Ideally, we would have liked to use the findings of this review to determine the predictive power of different neurocognitive tasks in terms of repetition of self-harm. However, in general, where studies determined that there was no association between a neurocognitive factor and repetition of self-harm, no statistics or detailed data were reported (e.g. five out of seven studies using MEPS, both studies using Go-Stop, the only study using TMT, two out of three studies using CPT). Therefore, making comments in terms of the negative predictive power of tasks is particularly difficult. Nonetheless, due to the variability seen in findings across studies for many tasks (such as the Emotional Stroop, CPT), the sensitivity and specificity is likely to be low. Furthermore, even with tasks that may show promise (such as the IAT, although this only involved one study), only 31.8% of those identified as potentially high risk (according to a strong association between death / suicide and self) actually repeated self-harm over 6 months. In other words, the false positive rate was approximately 68%. Therefore, the main strength of neurocognitive factors may prove to be in terms of identifying mechanisms for repetition of self-harm rather than as risk factors in isolation for prediction of repetition.

5. Conclusions

In conclusion, the evidence base is patchy and inconsistent for most neurocognitive factors in terms of potential associations with repetition of self-harm. Furthermore, the majority of data for problem solving, particularly using the MEPS measure, demonstrated no association with repetition of self-harm. However, there were some promising findings for certain neurocognitive factors and tasks. Therefore, further research and re-analyses of data for decision-making, emotional-processing, different memory domains, and aspects of cognitive control is recommended.

At this time, neurocognitive variables may be most appropriate for understanding the neural mechanisms underlying self-harm behaviour. However, combining variables may lead to future clinical applications, such as (i) enhanced risk assessments of self-harm to include bedside tests of specific neurocognitive factors (alongside demographics and clinical factors), and (ii) targeted treatment of individual neurocognitive deficits, potentially using tailored cognitive therapy, targeted neurophysiological techniques (e.g. brain stimulation) or pharmacotherapy (de Cates and Broome, 2016). Early intervention after episodes of self-harm or suicidal ideation in this targeted manner could potentially reduce the risk of these patients repeating self-harm and / or requiring longer term support from mental health services.

Acknowledgements

AdeC was in receipt of a National Institute for Health Research (NIHR) Academic Clinical Fellowship at the time of this review

KH is a National Institute for Health Research (NIHR) Senior Investigator

KR is supported by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care West Midlands

The NIHR had no other input into the research described or the drafting of this article.

Appendix

Appendix 1: Medline search strategy

1. deliberate self-harm.mp.
2. self-harm.mp.
3. deliberate self harm.mp.
4. suicid*.mp. or exp Self Mutilation/ or exp Suicide, Attempted/ or exp Self-Injurious Behavior/ or self harm.mp. or exp Suicide/
5. repet*.mp.
6. repeat*.mp.
7. persist*.mp.
8. predict*.mp.
9. decision making.mp. or exp Decision Making/
10. decision-making.mp.
11. decis*.mp.
12. exp Problem Solving/ or problem solving.mp. or problem-solving.mp.
13. cogniti*.mp.
14. aggress*.mp. or exp Aggression/ or exp Impulse Control Disorders/ or exp Impulsive Behavior/ or impuls*.mp.
15. emotion*.mp. or exp Emotions/ or exp Facial Expression/ or exp Arousal/ or exp Affect/
16. amygdala.mp. or exp Amygdala/
17. orbitofrontal cortex.mp. or exp Prefrontal cortex/
18. dorsolateral prefrontal cortex.mp.
19. anterior cingulate cortex.mp. or exp Gyrus Cinguli/
20. 1 or 2 or 3 or 4
21. 5 or 6 or 7 or 8
22. 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
23. 20 and 21 and 22

Appendix 2: Results of database searches

Medline search (4/3/15): 2145 results

Embase search (4/3/15): 4320 results

PsycINFO search (6/3/15): 249 results

CINAHL search (4/3/15): 647 results

The Cochrane Library search (4/3/15): 193 results

Web of Science search (4/3/15): 3571 results

Total results from all databases = 11125

Unique references after removal of duplicates = 6990

Study	Study type	SH assessment (definition)	Cognitive or self-assessment (measure)	Participants: number, M/F, age	Diagnosis	Length F/U	Loss to F/U	Repetition of SH - form	Repetition of SH - frequency
Blumberg 2014 **Adolescents** **USA**	Case-control imaging plus longitudinal F/U	Suicide attempt (not defined)	Imaging (fMRI) & cognitive emotional-processing (faces task)	n=unclear 51 suicide attempters; 63 affective controls; Unclear number HC	Affective disorder	Unclear	Not given	Repeaters vs non-repeaters over F/U	Not given

Key: SH = self-harm, M/F = male / female, F/U = follow-up, HC = healthy controls, N/A = not applicable, fMRI = functional magnetic resonance imaging, USA = United States

References

APA, 2015. Diagnostic and Statistical Manual of Mental Disorders (DSM). American Psychiatric Associatiation.

Arensman, E., Corocoran, P., Fitzgerald, A.P., 2011. Deliberate Self-Harm: Extent of the Problem and Prediction of Repetition, in: O'Connor, R.C., Platt, S., Gordon, J.R. (Eds.), International Handbook of Suicide Prevention. Wiley-Blackwell, Chichester, West Sussex.

Barzilay, S., Apter, A., 2014. Predictors of suicide in adolescents and adults with mood and common comorbid disorders. Neuropsychiatry 4, 81-93.

Benedetti, F., Radaelli, D., Poletti, S., Locatelli, C., Falini, A., Colombo, C., Smeraldi, E., 2011. Opposite effects of suicidality and lithium on gray matter volumes in bipolar depression. J Affect Disord 135, 139-147.

Blasco-Fontecilla, H., Baca-Garcia, E., Dervic, K., Perez-Rodriguez, M.M., Saiz-Gonzalez, M.D., Saiz-Ruiz, J., Oquendo, M.A., de Leon, J., 2009. Severity of personality disorders and suicide attempt. Acta Psychiatr Scand 119, 149-155.

Blumberg, H., 2014. Multimodality MRI evidence for altered frontal system trajectories in association with suicide attempts in adolescents: Common and distinct features across bipolar and major depressive disorders. Neuropsychopharmacol 39, S25.

Brent, D., 2011. Nonsuicidal self-injury as a predictor of suicidal behavior in depressed adolescents. Am J Psychiatry 168, 452-454.

Carroll, R., Metcalfe, C., Gunnell, D., 2014. Hospital management of self-harm patients and risk of repetition: systematic review and meta-analysis. J Affect Disord 168, 476-483.

Cha, C.B., Najmi, S., Park, J.M., Finn, C.T., Nock, M.K., 2010. Attentional Bias Toward Suicide-Related Stimuli Predicts Suicidal Behavior. J Abnorm Psychology 119, 616-622.

Chen, Y.W., Dilsaver, S.C., 1996. Lifetime rates of suicide attempts among subjects with bipolar and unipolar disorders relative to subjects with other Axis I disorders. Biol Psychiatry 39, 896-899.

Christiansen, E., Jensen, B.F., 2007. Risk of repetition of suicide attempt, suicide or all deaths after an episode of attempted suicide: a register-based survival analysis. Aust N Z J Psychiatry 41, 257-265.

Clark, L., Dombrovski, A.Y., Siegle, G.J., Butters, M.A., Shollenberger, C.L., Sahakian, B.J., Szanto, K., 2011. Impairment in risk-sensitive decision-making in older suicide attempters with depression. Psychol Aging 26, 321-330.

Collinson, M., Owens, D., Blenkiron, P., Burton, K., Graham, L., Hatcher, S., House, A., Martin, K., al., e., 2014. MIDSHIPS: multicentre intervention designed for self-harm using interpersonal problem-solving: protocol for a randomised controlled feasibility study. Trials 15, 163.

Cona, G., Treccani, B., Umilta, C.A., 2016. Is cognitive control automatic? New insights from transcranial magnetic stimulation. Psychon Bull Rev.

Cooper, J., Steeg, S., Webb, R., Stewart, S.L., Applegate, E., Hawton, K., Bergen, H., Waters, K., al., e., 2013. Risk factors associated with repetition of self-harm in black and minority ethnic (BME) groups: a multi-centre cohort study. J Affect Disord 148, 435-439.

Cox Lippard, E.T., Johnston, J.A., Blumberg, H.P., 2014. Neurobiological risk factors for suicide: insights from brain imaging. Am J Prev Med 47, S152-162.

Criaud, M., Boulinguez, P., 2013. Have we been asking the right questions when assessing response inhibition in go/no-go tasks with fMRI? A meta-analysis and critical review. Neurosci Biobehav Rev 37, 11-23.
D'Zurilla, T.J., Chang, E.C., Nottingham, I.E.J., Faccini, L., 1998. Social problem-solving deficits and hopelessness, depression, and suicidal risk in college students and psychiatric inpatients. J Clin Psychology 54, 1091-1107.
de Cates, A.N., Broome, M.R., 2016. Can we use neurocognition to predict repetition of self-harm, and why might this be clinically useful? A perspective. Front Psychiatry 7.
De Leo, D., Padoani, W., Scocco, P., Lie, D., Bille-Brahe, U., Arensman, E., Hjelmeland, H., Crepet, P., al., e., 2001. Attempted and completed suicide in older subjects: results from the WHO/EURO Multicentre Study of Suicidal Behaviour. Int J Geriatr Psychiatry 16, 300-310.
Dieserud, G., Røysamb, E., Braverman, M.T., Dalgard, O.S., Ekeberg, Ø., 2003. Predicting repetition of suicide attempt: A prospective study of 50 suicide attempters. Archiv Suicide Res 7, 1-15.
Dixon, M.L., Christoff, K., 2014. The lateral prefrontal cortex and complex value-based learning and decision making. Neurosci Biobehav Rev 45, 9-18.
Dougherty, D.M., Mathias, C.W., Marsh, D.M., Papageorgiou, T.D., Swann, A.C., Moeller, F.G., 2004. Laboratory measured behavioral impulsivity relates to suicide attempt history. Suicide Life Threat Behav 34, 374-385.
Egner, T., Hirsch, J., 2005. Cognitive control mechanisms resolve conflict through cortical amplification of task-relevant information. Nat Neurosci 8, 1784-1790.
Fikke, L.T., Melinder, A., Landro, N.I., 2011. Executive functions are impaired in adolescents engaging in non-suicidal self-injury. Psychol Med 41, 601-610.
Fliege, H., Lee, J.R., Grimm, A., Klapp, B.F., 2009. Risk factors and correlates of deliberate self-harm behavior: A systematic review. J Psychosom Res 66, 477-493.
Gifuni, A.J., Ding, Y., Olie, E., Lawrence, N., Cyprien, F., Le Bars, E., Bonafe, A., Phillips, M.L., Courtet, P., Jollant, F., 2016. Subcortical nuclei volumes in suicidal behavior: nucleus accumbens may modulate the lethality of acts. Brain Imaging Behav 10, 96-104.
Glascher, J., Adolphs, R., Damasio, H., Bechara, A., Rudrauf, D., Calamia, M., Paul, L.K., Tranel, D., 2012. Lesion mapping of cognitive control and value-based decision making in the prefrontal cortex. Proc Natl Acad Sci U S A 109, 14681-14686.
Glenn, C.R., Nock, M.K., 2014. Improving the short-term prediction of suicidal behavior. Am J Prevent Med 47, S176-S180.
Goldston, D.B., Daniel, S.S., Reboussin, B.A., Reboussin, D.M., Frazier, P.H., Harris, A.E., 2001. Cognitive risk factors and suicide attempts among formerly hospitalized adolescents: A prospective naturalistic study. J Am Acad Child Adolesc Psychiatry 40, 91-99.
Gorlyn, M., 2005. Impulsivity in the prediction of suicidal behavior in adolescent populations. Int J Adolesc Med Health 17, 205-209.
Groschwitz, R.C., Plener, P.L., Kaess, M., Schumacher, T., Stoehr, R., Boege, I., 2015. The situation of former adolescent self-injurers as young adults: a follow-up study. BMC Psychiatry 15, 160.
Han, S., Northoff, G., 2009. Understanding the self: a cultural neuroscience approach. Prog Brain Res 178, 203-212.
Hatcher, S., Sharon, C., House, A., Collins, N., Collings, S., Pillai, A., 2015. The ACCESS study: Zelen randomised controlled trial of a package of care for people presenting to hospital after self-harm. Br J Psychiatry 206, 229-236.

Hawton, K., 2012. Psychiatric assessment and management of deliberate self-poisoning patients. Medicine 40, 71-73.
Hawton, K., Casey, D., Bale, E., Ryall, J., Geulayov, G., Brand, F., 2015. Self-harm in Oxford 2013. Centre for Suicide Research, Oxford.
Hawton, K., Comabella, C.C.I., Haw, C., Saunders, K., 2013. Risk factors for suicide in individuals with depression: A systematic review. Journal of Affective Disorders, 147, 17-28. . J Affect Disord 147, 17-28.
Hawton, K., Kingsbury, S., Steinhardt, K., James, A., Fagg, J., 1999. Repetition of deliberate self-harm by adolescents: The role of psychological factors. J Adolesc 22, 369-378.
Hawton, K., Saunders, K.E., O'Connor, R.C., 2012. Self-harm and suicide in adolescents. Lancet 379, 2373-2382.
Hawton, K., van Heeringen, K., 2009. Suicide. Lancet 373, 1372-1381.
Higgins, J.P., Green, S., 2011. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. The Cochrane Collaboration.
Hughes, S.L., Neimeyer, R.A., 1993. Cognitive predictors of suicide risk among hospitalized psychiatric patients: A prospective study. Death Studies 17, 103-124.
Husain, N., Chaudhry, N., Durairaj, S.V., Chaudhry, I., Khan, S., Husain, M., Nagaraj, D., Naeem, F., al., e., 2011. Prevention of self harm in British South Asian women: study protocol of an exploratory RCT of culturally adapted manual assisted Problem Solving Training (C- MAP). Trials 12.
Jollant, F., 2016. Neuroimaging of Suicidal Behavior, in: Kaschka, W.P., Rujescu, D. (Eds.), Biological Aspects of Suicidal Behavior. Adv Biol Psychiatry. Karger, pp. 110-122.
Jollant, F., Bellivier, F., Leboyer, M., Astruc, B., Torres, S., Verdier, R., Castelnau, D., Malafosse, A., Courtet, P., 2005. Impaired decision making in suicide attempters. Am J Psychiatry 162, 304-310.
Jollant, F., Guillaume, S., Jaussent, I., Castelnau, D., Malafosse, A., Courtet, P., 2008a. Characterization of decision-making impairment in suicide attempters and the influence of attention to wins on suicidal intent and repetition. Biol Psychiatry 63, 292S-292S.
Jollant, F., Lawrence, N.L., Olie, E., Guillaume, S., Courtet, P., 2011. The suicidal mind and brain: A review of neuropsychological and neuroimaging studies. World J Biol Psychiatry 12, 319-339.
Jollant, F., Lawrence, N.S., Giampietro, V., Brammer, M.J., Fullana, M.A., Drapier, D., Courtet, P., Phillips, M.L., 2008b. Orbitofrontal cortex response to angry faces in men with histories of suicide attempts. Am J Psychiatry 165, 740-748.
Jollant, F., Lawrence, N.S., Olie, E., O'Daly, O., Malafosse, A., Courtet, P., Phillips, M.L., 2010. Decreased activation of lateral orbitofrontal cortex during risky choices under uncertainty is associated with disadvantageous decision-making and suicidal behavior. Neuroimage 51, 1275-1281.
Kehrer, C.A., Linehan, M.M., 1996. Interpersonal and emotional problem solving skills and parasuicide among women with borderline personality disorder. J Personality Disord 10, 153-163.
Keilp, J.G., Beers, S.R., Burke, A.K., Melhem, N.M., Oquendo, M.A., Brent, D.A., Mann, J.J., 2014. Neuropsychological deficits in past suicide attempters with varying levels of depression severity. Psychol Med 44, 2965-2974.
Larkin, C., Di Blasi, Z., Arensman, E., 2013. Self-cutting versus intentional overdose: psychological risk factors. Med Hypotheses 81, 347-354.

Larkin, C., Di Blasi, Z., Arensman, E., 2014. Risk factors for repetition of self-harm: A systematic review of prospective hospital-based studies. PLoS ONE 9.
Liberati, A., Altman, D.G., Tetzlaff, J., Mulrow, C., Gotzsche, P.C., Ioannidis, J.P., Clarke, M., Devereaux, P.J., al., e., 2009. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med 6, e1000100.
Liu, X.H., Li, L., Xiao, J., Yang, J., Jiang, X.Q., 2013. Abnormalities of autobiographical memory of patients with depressive disorders: A meta-analysis. Psychol Psychother 86, 353-373.
Lu, C.H., Proctor, R.W., 1995. The influence of irrelevant location information on performance: A review of the Simon and spatial Stroop effects. Psychon Bull Rev 2, 174-207.
Malloy-Diniz, L.F., Neves, F.S., Abrantes, S.S., Fuentes, D., Correa, H., 2009. Suicide behavior and neuropsychological assessment of type I bipolar patients. J Affect Disord 112, 231-236.
Mann, J.J., Apter, A., Bertolote, J., Beautrais, A., Currier, D., Haas, A., Hegerl, U., Lonnqvist, J., al., e., 2005. Suicide prevention strategies: a systematic review. JAMA 294, 2064-2074.
Martinez-Aran, A., Vieta, E., Reinares, M., Colom, F., Torrent, C., Sanchez-Moreno, J., Benabarre, A., Goikolea, J.M., Comes, M., Salamero, M., 2004. Cognitive function across manic or hypomanic, depressed, and euthymic states in bipolar disorder. Am J Psychiatry 161, 262-270.
Mathias, C.W., Dougherty, D.M., James, L.M., Richard, D.M., Dawes, M.A., Acheson, A., Hill-Kapturczak, N., 2011. Intolerance to Delayed Reward in Girls with Multiple Suicide Attempts. Suicide Life Threat Behav 41, 277-286.
McAuliffe, C., Corcoran, P., Hickey, P., McLeavey, B.C., 2008. Optional thinking ability among hospital-treated deliberate self-harm patients: a 1-year follow-up study. Br J Clin Psychol 47, 43-58.
McAuliffe, C., Corcoran, P., Keeley, H.S., Arensman, E., Bille-Brahe, U., de Leo, D., Fekete, S., Hawton, K., al., e., 2006. Problem-solving ability and repetition of deliberate self-harm: A multicentre study. Psychol Med 36, 45-55.
McAuliffe, C., McLeavey, B.C., Fitzgerald, T., Corcoran, P., Carroll, B., Ryan, L., O'Keeffe, B., Fitzgerald, E., Hickey, P., O'Regan, M., Mulqueen, J., Arensman, E., 2014. Group problem-solving skills training for self-harm: randomised controlled trial. Br J Psychiatry 204, 383-390.
Mendez-Bustos, P., De Leon-Martinez, V., Miret, M., Baca-Garcia, E., Lopez-Castroman, J., 2013. Suicide reattempters: A systematic review. Harvard Rev Psychiatry 21, 281-295.
Miranda, R., Gallagher, M., Bauchner, B., Vaysman, R., Marroquin, B., 2012. Cognitive inflexibility as a prospective predictor of suicidal ideation among young adults with a suicide attempt history. Depress Anxiety 29, 180-186.
Monkul, E.S., Hatch, J.P., Nicoletti, M.A., Spence, S., Brambilla, P., Lacerda, A.L., Sassi, R.B., Mallinger, A.G., al., e., 2007. Fronto-limbic brain structures in suicidal and non-suicidal female patients with major depressive disorder. Mol Psychiatry 12, 360-366.
Monnin, J., Thiemard, E., Vandel, P., Nicolier, M., Tio, G., Courtet, P., Bellivier, F., Sechter, D., al., e., 2012. Sociodemographic and psychopathological risk factors in repeated suicide attempts: Gender differences in a prospective study. J Affect Disord 136, 35-43.

NCISH, 2015. National Confidential Inquiry into Suicide and Homicide by People with Mental Illness. University of Manchester, Manchester.
NICE, 2011. Self-harm: longer term management. National Institute of Clinical Excellence, London.
Nock, M.K., Park, J.M., Finn, C.T., Deliberto, T.L., Dour, H.J., Banaji, M.R., 2010. Measuring the suicidal mind: Implicit cognition predicts suicidal behavior. Psychological Science 21, 511-517.
Oldershaw, A., Grima, E., Jollant, F., Richards, C., Simic, M., Taylor, L., Schmidt, U., 2009. Decision making and problem solving in adolescents who deliberately self-harm. Psychol Med 39, 95-104.
Owens, D., Horrocks, J., House, A., 2002. Fatal and non-fatal repetition of self-harm. Systematic review. Br J Psychiatry 181, 193-199.
Owens, D., Kelley, R., Munyombwe, T., Bergen, H., Hawton, K., Cooper, J., Ness, J., Waters, K., al., e., 2015. Switching methods of self-harm at repeat episodes: Findings from a multicentre cohort study. J Affect Disord 180, 44-51.
Pan, L.A., Hassel, S., Segreti, A.M., Nau, S.A., Brent, D.A., Phillips, M.L., 2013. Differential patterns of activity and functional connectivity in emotion processing neural circuitry to angry and happy faces in adolescents with and without suicide attempt. Psychol Med 43, 2129-2142.
Platt, S., Bille-Brahe, U., Kerkhof, A., Schmidtke, A., Bjerke, T., Crepet, P., De Leo, D., Haring, C., Lonnqvist, J., Michel, K., et al., 1992. Parasuicide in Europe: the WHO/EURO multicentre study on parasuicide. I. Introduction and preliminary analysis for 1989. Acta Psychiatr Scand 85, 97-104.
Pluck, G., Lekka, N.P., Sarkar, S., Lee, K.H., Bath, P.A., Sharif, O., Woodruff, P.W.R., 2013. Clinical and neuropsychological aspects of non-fatal self-harm in schizophrenia. Eur Psychiatry 28, 344-348.
Pollock, L.R., Williams, J.M., 2001. Effective problem solving in suicide attempters depends on specific autobiographical recall. Suicide Life Threat Behav 31, 386-396.
Pollock, L.R., Williams, J.M.G., 2004. Problem-solving in suicide attempters. Psychol Med 34, 163-167.
Quinlivan, L., Cooper, J., Davies, L., Hawton, K., Gunnell, D., Kapur, N., 2016. Which are the most useful scales for predicting repeat self-harm? A systematic review evaluating risk scales using measures of diagnostic accuracy. BMJ Open 6, e009297.
Randall, J.R., Colman, I., Rowe, B.H., 2011. A systematic review of psychometric assessment of self-harm risk in the emergency department. J Affect Disord 134, 348-355.
Rasmussen, S.A., O'Connor, R.C., Brodie, D., 2008. The role of perfectionism and autobiographical memory in a sample of parasuicide patients: an exploratory study. Crisis 29, 64-72.
Richard-Devantoy, S., Berlim, M.T., Jollant, F., 2014a. A meta-analysis of neuropsychological markers of vulnerability to suicidal behavior in mood disorders. Psychol Med 44, 1663-1673.
Richard-Devantoy, S., Berlim, M.T., Jollant, F., 2015. Suicidal behaviour and memory: A systematic review and meta-analysis. World J Biol Psychiatry 16, 544-566.
Richard-Devantoy, S., Ding, Y., Lepage, M., Turecki, G., Jollant, F., 2016a. Cognitive inhibition in depression and suicidal behavior: a neuroimaging study. Psychol Med 46, 933-944.

Richard-Devantoy, S., Guillaume, S., Olie, E., Courtet, P., Jollant, F., 2013a. Altered explicit recognition of facial disgust associated with predisposition to suicidal behavior but not depression. J Affect Disord 150, 590-593.
Richard-Devantoy, S., Jollant, F., Kefi, Z., Turecki, G., Olie, J.P., Annweiler, C., Beauchet, O., Le Gall, D., 2012. Deficit of cognitive inhibition in depressed elderly: a neurocognitive marker of suicidal risk. J Affect Disord 140, 193-199.
Richard-Devantoy, S., Olie, E., Guillaume, S., Bechara, A., Courtet, P., Jollant, F., 2013b. Distinct alterations in value-based decision-making and cognitive control in suicide attempters: toward a dual neurocognitive model. J Affect Disord 151, 1120-1124.
Richard-Devantoy, S., Olie, E., Guillaume, S., Courtet, P., 2016b. Decision-making in unipolar or bipolar suicide attempters. J Affect Disord 190, 128-136.
Richard-Devantoy, S., Orsat, M., Dumais, A., Turecki, G., Jollant, F., 2014b. Neurocognitive vulnerability: suicidal and homicidal behaviours in patients with schizophrenia. Can J Psychiatry 59, 18-25.
Rodham, K., Hawton, K., Evans, E., 2004. Reasons for deliberate self-harm: comparison of self-poisoners and self-cutters in a community sample of adolescents. J Am Acad Child Adolesc Psychiatry 43, 80-87.
Saunders, K., Brand, F., Lascelles, K., Hawton, K., 2014. The sad truth about the SADPERSONS Scale: an evaluation of its clinical utility in self-harm patients. Emerg Med J 31, 796-798.
Sinclair, J.M.A., Crane, C., Hawton, K., Williams, J.M.G., 2007. The role of autobiographical memory specificity in deliberate self-harm: Correlates and consequences. J Affect Disord 102, 11-18.
Sinclair, J.M.A., Gray, A., Rivero-Arias, O., Saunders, K.E.A., Hawton, K., 2011. Healthcare and social services resource use and costs of self-harm patients. Soc Psychiatry Psychiatr Epidemiol 46, 263-271.
Swann, A.C., Dougherty, D.M., Pazzaglia, P.J., Pham, M., Steinberg, J.L., Moeller, F.G., 2005. Increased impulsivity associated with severity of suicide attempt history in patients with bipolar disorder. Am J Psychiatry 162, 1680-1687.
Tejedor, M.C., Diaz, A., Castillon, J.J., Pericay, J.M., 1999. Attempted suicide: repetition and survival--findings of a follow-up study. Acta Psychiatr Scand 100, 205-211.
Van Heeringen, C., Bijttebier, S., Godfrin, K., 2011. Suicidal brains: a review of functional and structural brain studies in association with suicidal behaviour. Neurosci Biobehav Rev 35, 688-698.
van Heeringen, K., 2003. The neurobiology of suicide and suicidality. Can J Psychiatry 48, 292-300.
van Heeringen, K., Bijttebier, S., Desmyter, S., Vervaet, M., Baeken, C., 2014. Is there a neuroanatomical basis of the vulnerability to suicidal behavior? A coordinate-based meta-analysis of structural and functional MRI studies. Front Hum Neurosci 8, 824.
van Heeringen, K., Mann, J.J., 2014. The neurobiology of suicide. Lancet Psychiatry 1, 63-72.
von Elm, E., Altman, D.G., Egger, M., Pocock, S.J., Gotzsche, P.C., Vandenbroucke, J.P., Initiative, S., 2007. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet 370, 1453-1457.
Walter, H., 2013. The third wave of biological psychiatry. Front Psychol 4, 582.

Westheide, J., Quednow, B.B., Kuhn, K.U., Hoppe, C., Cooper-Mahkorn, D., Hawellek, B., Eichler, P., Maier, W., Wagner, M., 2008. Executive performance of depressed suicide attempters: the role of suicidal ideation. Eur Arch Psychiatry Clin Neurosci 258, 414-421.
WHO, 2012. Public Health Action for the Prevention of Suicide. World Health Organisation, Geneva.
WHO, 2015. WHO Mortality Database: Suicide. World Health Organisation, Geneva.
Wilkinson, P., Kelvin, R., Roberts, C., Dubicka, B., Goodyer, I., 2011. Clinical and psychosocial predictors of suicide attempts and nonsuicidal self-injury in the Adolescent Depression Antidepressants and Psychotherapy Trial (ADAPT). Am J Psychiatry 168, 495-501.
Zahl, D.L., Hawton, K., 2004. Repetition of deliberate self-harm and subsequent suicide risk: long-term follow-up study of 11,583 patients. Br J Psychiatry 185, 70-75.

Figure Captions

Figure 1: PRISMA flow diagram

PRISMA diagram to demonstrate the flow of studies in the systematic review