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Neurocognitive functioning and impulsivity in first-episode psychosis with suicidal ideation and behavior: a systematic review

Emmanuel Diaz

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UNIVERSITE DE MONTPELLIER
FACULTE DE MEDECINE MONTPELLIER-NIMES

THESE

Pour obtenir le titre de
DOCTEUR EN MEDECINE

Présentée et soutenue publiquement

Par

Emmanuel DIAZ

le 1^{er} décembre 2020

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suicidal ideation and behavior: a systematic review

Directeur de thèse : Monsieur le Professeur Jorge Lopez Castroman

JURY

Président :

Monsieur le Professeur Philippe Courtet

Assesseurs :

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Introduction en français

Les idées et comportements suicidaires sont fréquents avant et près de l'entrée dans un premier épisode psychotique (PEP). Lors du premier contact avec une unité de soins psychiatriques des patients avec PEP, la prévalence des idées suicidaires retrouvée dans la littérature varie entre 21 et 50% (1–4). La prévalence est de 70% si il est considéré la durée totale de psychose non traitée (4). Elles pourraient persister pour plus d'un tiers des patients jusqu'à 10 ans de suivi (5). La présence d'idées suicidaires lors des premiers contacts avec une unité de soins psychiatriques serait associée à un risque environ cinq fois plus élevé de tentative de suicide à un an (6). Entre 18 et 26% des patients passent à l'acte avant ce premier contact (4,6) et 2,9 à 18,2 % des patients après l'entrée dans un PEP (7). Enfin il est rapporté entre 0,4 à 4,3% de décès par suicide après cette transition (7) soit 12 fois plus important que dans la population générale (8). De plus, le taux de conduites suicidaires est plus important lorsque proche du début du PEP, particulièrement la première année (8) voire les six premiers mois (9).

L'intensité des idées suicidaires au début du PEP peut être un facteur prédictif du risque de passage à l'acte (10). En effet il est possible de retranscrire l'évolution des idées suicidaires en 3 trajectoires selon la fréquence de l'idéation l'année précédant le contact médical. Ceux présentant une fréquence faible (une à quelques fois) vont à terme avoir plutôt une régression des idées suicidaires. Ceux présentant des fréquences plus élevées ont 4,5 fois plus de chance d'avoir encore des idées suicidaires à 5 ans de suivi et environ 4 fois plus à 10 ans que ceux présentant des fréquences faibles. Ces patients réaliseront 2,8 et 6,6 fois plus de tentatives de suicide respectivement à 5 et 10 ans de suivi. Le PEP est ainsi une période de transition critique sur le plan suicidaire. Cela justifie l'intérêt de l'évaluation du risque suicidaire et de développer la recherche sur des facteurs associés à des fins de dépistage et prévention.

Des altérations cognitives telles qu'un déficit en quotient intellectuel (11), fonctions exécutives (11,12), mémoire verbale (11,13), vitesse de traitement (13,14), cognition sociale et émotionnelle (15,16) et théorie de l'esprit (16,17) sont retrouvées parmi les patients avec PEP.

Certaines études ont trouvé une association entre déficit neuropsychologique et le syndrome clinique négatif de la schizophrénie (18) ou bien encore avec le retentissement fonctionnel (19,20). Ces anomalies auraient probablement une stabilité dans le temps (21–23) avec un profil similaire d'une schizophrénie évoluée (24). L'exposition importante des patients avec PEP au risque suicidaire pourrait s'expliquer en partie par rapport aux altérations neurocognitives retrouvées chez ces patients. En effet les conduites suicidaires ont déjà été appréhendées sur le versant neuropsychologique (25) avec des altérations pouvant peut être les expliquer partiellement. D'ailleurs des anomalies neuropsychologiques peuvent être retrouvées dans plusieurs troubles psychiatriques associés a un risque suicidaire accru, tels que les troubles de la personnalité borderline (26) ou les troubles de l'humeur (27). Concernant la schizophrénie, certaines études n'ont pas mis en évidence d'anomalies plus marquées chez les patients présentant des conduites suicidaires (28–30) et certaines retrouvent des fonctions cognitives moins détériorées (31–33). D'autres études concluent à des fonctions cognitives sociales et émotionnelles (reconnues comme endophénotype et marqueur de vulnérabilité à une entrée dans un PEP chez des sujets prodromaux) plus détériorées chez les patients présentant des conduites suicidaires ou idées suicidaires isolées (34–36). Enfin une plus grande impulsivité peut être associée à la présence d'idées suicidaires et la réalisation de tentative de suicide (37) ou suicides aboutis (38).

Ainsi les patients avec un PEP présentent des altérations cognitives et sont à risque de conduites suicidaires. D'une manière générale des altérations cognitives dont une impulsivité plus marquée sont retrouvées chez les patients suicidants. Ces altérations peuvent être d'autant plus prononcées chez les patients suicidants parmi les patients atteints de trouble bipolaire ou schizophrénique : les deux principales évolutions du PEP. L'objectif de cette revue systématique de la littérature est de faire l'état des connaissances sur une éventuelle association entre des altérations neurocognitives ou comportements impulsifs et la présence d'idées suicidaires ou conduites suicidaires chez des patients avec un PEP.

Abstract

Background:

The prevalence of suicidal ideation (SI) and behavior (SB) among people suffering from psychotic disorders is a major public health issue. Most suicide attempts (SAs) occur before or during the early phases of first-episode psychosis (FEP). Improving knowledge about the suicide risk in the early stages of illness is essential to develop therapeutic and prevention strategies. We conducted a systematic review of the literature to investigate an association between neurocognitive impairments or a history of impulsive behavior, and SI or SB among patients with FEP.

Method:

PRISMA guidelines were followed. Ten databases were searched, notably PubMed, using MeSH terms or key-words related to first-episode psychosis, impulsivity or cognitive functioning measures and SI or SB. A narrative summary was used to report our findings.

Results:

Ten research papers were included from the databases searched and also six supplementary articles from bibliographic references or expert opinions. Five studies showed more pronounced neuropsychological impairments, especially regarding attention, processing speed, executive functioning and theory of mind for patients with FEP who commit SAs. So far no studies have found an association between cognitive deficits on neuropsychological tests and SI. Previous non-suicidal impulsive behaviors have been found to be associated with SAs and suicide.

Conclusion:

Our review suggests an association between neuropsychological impairments and SAs among patients with FEP. Moreover an association was found between impulsive behavior and SB. Future research on the neuropsychology of FEP is warranted to identify how these impairments facilitate SB and evaluate their potential utility as therapeutic targets.

Introduction

Suicidal ideation (SI) and suicidal behavior (SB) are common before and during the early phases of first-episode psychosis (FEP). In the literature, a prevalence of 21 to 50% of SI is found during the first contact with FEP patients at a psychiatric care unit (1–4) and 70% during untreated psychosis (4). For more than a third of patients, SI may persist for up to 10 years of follow-up (5). SI is associated with approximately five times a greater risk of attempted suicide at one year (and also at two years) (6). 18 to 26% of patients with SB, attempt suicide before their first contact with a psychiatrist (4,6) then 2.9 to 18.2 % after the start of FEP (7). Lastly, 0.4 to 4.3% of deaths by suicide have been reported after this transition (7) which is 12 times higher than in the general population (8). Furthermore, the rate of SB increases as patients approach the beginning of FEP, especially during the first year (8) or the first six months (9).

The intensity of SI at the start of FEP may be a predictive factor of suicide attempts (SAs) (10). Indeed, it is possible to retranscribe the evolution of SI into three trajectories according to the frequency of ideation in the year preceding medical contact. Those with a low frequency (one to a few times) will eventually see a regression in their SI. Those who have the highest frequencies are 4.5 times more likely to still have SI at 5 years of follow-up and around 4 times more likely at 10 years of follow-up than those with lower frequencies. These patients will make 2.8 and 6.6 times more SAs at 5 and 10 years respectively. FEP is thus a critical transition period towards SI, justifying the interest of evaluating the risk of suicide and developing research on the factors associated with it, in order to screen for and prevent it.

Concerning cognitive impairments, deficits in IQ (11), executive functioning (11,12), verbal memory (11,13), processing speed (13,14), social and emotional cognition (15,16) and deficit in theory of mind (16,17) have been described in patients with FEP. Some studies have found an association between neuropsychology and negative syndrome (18) or psychosocial functioning (19,20). These anomalies would probably become quite stable over time (21–23) with a similar profile to that of permanent schizophrenia (24). The high exposure of patients with FEP

to the risk of suicide might be partly explained by the neurocognitive impairment found in them. Indeed, SB has already been apprehended from a neuropsychological aspect (25) with impairment possibly offering a partial explanation with this approach. Besides, neuropsychological anomalies may be found in several psychiatric disorders associated with an increased risk of SB, such as borderline personality disorder (26) and affective disorders (27). As for schizophrenia, some studies do not elucidate more marked anomalies in patients with SB (28–30) and some studies have found less deteriorated cognitive functioning among suicide attempters (31–33). Other studies conclude that social and emotional cognitive functioning (recognized as an endophenotype and vulnerability marker in prodromal subjects) is more deteriorated in patients with SB or those who have isolated suicidal thoughts (34–36). Lastly, greater impulsivity might be associated with SI and SAs (37) or completed suicides (38).

Patients with FEP therefore have cognitive impairments and are more likely to have SB. Cognitive impairments, including greater impulsivity, are found in suicidal patients. These may be even more pronounced among suicidal patients suffering from bipolar disorder or schizophrenia; the two main evolutions of FEP. The purpose of this systematic literature review was to take stock of the current state of knowledge on the role of neurocognitive impairments and impulsivity in SB and SI of patients with FEP.

Method

Search strategy

The protocol for the systematic review was registered at the PROSPERO Centre for Reviews and Dissemination (ID CRD42020177983) and designed according to PRISMA guidelines (39). The databases were searched from database creation to October 26th, 2019 using PubMed, Web of Science, Science Direct, PsycInfo, PsychArticles, Academic Search Premier, Pascal and Francis, PubPsych, Base Santé Psy and The Cochrane Library as search interfaces.

The keywords or MeSH terms used with the PubMed database were : (“First Episode Psychosis” OR “first episode schizophrenia” OR “recent onset schizophrenia” OR “recent onset psychosis”) AND (“neuropsych*” OR “mental processes” OR “cogniti*” OR “impulsiv*”) AND “suicid*”. For the other databases the search was made using the expressions “First Episode Psychosis” (or alternative term) AND “neuropsychology” (or alternative term) AND “suicide” (or alternative term). See appendix for details per database. Other studies were visually identified from reference lists of articles that met the inclusion criteria.

Inclusion and exclusion criteria

Studies had to be written in English or French. There were no restrictive criteria regarding the year of publication or the country and there were no restrictions regarding study design or length of follow-up either. All literature reviews or articles citing data from another article were excluded.

Only studies performed on samples of patients with FEP were included. Concerning the definition of FEP used for this review, we included all patients at early psychotic illness (treated psychosis included) except patients at risk (prodromal phase). Patients were either described directly by the authors as patients with FEP or recently diagnosed with schizophrenia or patients with psychotic symptoms upon first contact with a psychiatrist.

The studies included had to contain at least one combination of:

- 1) An evaluation via neuropsychological tests or validated questionnaires for at least one cognitive function or impulsivity measures. Studies noting a history of impulsive behavior as a proxy of impulsivity were also included. Indeed, a history of violence, particularly self-injurious behavior, was considered as a measure of impulsivity (association noticed in the literature in the study by Glenn and Klonsky (40) for example).

And:

- 2) The presence of SI, SAs or a suicide outcome.

Results of the systematic search

The studies obtained from the databases and bibliographic references of the studies included were selected with the agreement of two authors (JLC and ED). Titles and abstracts of the 130 screened studies were evaluated for eligibility. The complete article was thoroughly read if an evaluation of cognitive functioning was evoked in the abstract. The number of cognitive functions examined and the heterogeneity of the evaluations made it impossible to do a meta-analysis with such a small number of studies.

Data extraction and quality assessment

The data extracted were: the author, year of publication, country, sample size, age, sex, inclusion criteria (see Table 1), measurement of symptoms, measurement of suicidal ideation, measurement of suicidal behavior, neuropsychological test measurements and measurement of impulsivity or impulsivity-related behavior (see Table 3).

Each study was evaluated by two authors (ED and CE or AS) according to the Effective Public Health Practice Project Tool (41) to evaluate the risk of a possible bias. The differences were discussed until a consensus was reached. Biases were classified as either “weak”, “moderate” or “strong” for the overall score and individual categories. Details of biases for each study and per item can be found in Table 2.

Results

Studies selected

The initial database search gave 175 results. After removing all duplicates and applying the inclusion and non-inclusion criteria, ten studies were retained. From the reference list of these included studies, five more were added. One study, not found by the search equation due to a spelling mistake in a keyword was also added following expert opinion (JLC) (42). See flow chart (Fig. 1).

Study design and characteristics

Study design, mean duration of follow-up, countries of inclusion and sample characteristics (size, mean age, male percentage) are summarized in Table 1. Concerning the population under study, seven previous studies had described their population as “first episode psychosis” patients. Other studies had used alternative expressions found in Table 1. Each study used its own inclusion criteria (see Appendix).

The outcomes on neuropsychological or psychological measurements, impulsive behavior, and suicide are summarized in Table 3. Six studies sought predictive characteristics for SAs by taking into account only SAs made after clinical evaluation of the judgement criteria (38,42–46) and 6 studies took into account SAs up to the evaluation (47–52). One study included both SAs made before the evaluation and those made during follow-up (53).

Quality assessment

Biases are summarized in Table 2.

The main biases are related to: (i) the type of study design with a low level of evidence (mainly transversal studies), (ii) the selection of patients without randomization, (iii) the lack of information on whether (and if so, how) the clinical or neuropsychological evaluations were blinded and (iv) the absence of an adjustment on clinical confounding factors such as the severity of depression.

Indeed, according to the Effective Public Health Practice Project Tool (41), 14 studies in all were considered as having a strong bias, 2 studies as having a moderate bias and no study as having a weak bias. The results for SI, SB, SAs and suicide are summarized in Table 3.

Suicidal ideation

One study of 89 patients (1) found significantly greater impulsivity according to the Barratt Impulsiveness Scale for “attentional impulsiveness” in patients with SI. However, no difference was found using the Hayling Sentence Completion Test (which also measures both impulsivity and executive functioning). Executive functioning also proved not to differ in suicidal ideation according to the Wisconsin Card Sorting Test. Another Chinese study (54) concluded that patients presenting FEP with SI during the two weeks prior to clinical evaluation had a less marked working memory deficiency (letter 2-back task) and verbal comprehension deficiency (Information Symbol subtest of Wechsler Adult Intelligence Scale-Chinese Revised) than those without SI. The authors found less cognitive impairment despite patients with SI being more depressed than those without SI according to the Calgary Depression Scale for Schizophrenia. In contrast, one American study on 35 patients found no difference in reaction time with the Continuous Performance Task (AX-version) between patients with or without SI. In that study, the Continuous Performance Task reflected attentional capacities (50).

Two studies used an overall variable for suicidality or the risk of suicide. A German study on 152 patients (49) found a correlation between suicidality at the time of admission and a deficiency in executive functioning, capacity for concentration, attention and IQ. However there was a loss of significance for the sum total of all the tests. The neuropsychological tests performed were, respectively, the Wisconsin Card Sorting Test, the d2 test, the Testbatterie zur Aufmerksamkeitsprüfung, the divided attention and Go-Nogo subtests, and lastly, the revised Hamburg-Wechsler Adult Intelligence Scale (HaWIE-R Intelligence Quotient). The other Chinese study on 33 patients with FEP (48) found no difference in patients with a higher score on the Schizophrenia Suicide Risk Scale with the n-back test. Thus, to resume, impulsivity might be higher in patients with SI among FEP patients, and contradictory results are found for attentional and executive functioning.

Attempted suicide

The most recent study on attempted suicide including 517 patients (42) showed an association between a lower overall cognitive performance and patients with SB (effect size: 0.58). Patients underwent a battery of tests covering all the main cognitive functions. Separately, an association was only found for more impaired processing speed (WAIS-III Digit Symbol subtest) and motor dexterity (Grooved Pegboard Handedness) among patients with SB. Another study by the same author (46) assessing theory of mind showed a correlation between SAs and theory of mind deficiency with an odds ratio of 4.3 (first-order false belief task).

One study (52) only noted better attentional performance among suicidal patients (Digit Span and Coding tasks). Conversely, the study by Minzenberg (51) found a greater reaction time during the Stroop Task Performance test in suicidal patients. Executive functioning, also evaluated by the Stroop Task Performance test, did not discriminate suicidal patients in this study, nor did using the Trail-Making Test A and B (as well as processing speed) in the study by Lopez-Morinigo (45). IQ was not discriminating either (45). Finally, with a complete battery of neuropsychological tests, the study by Ayesa-Arriola (53) only found one difference among patients with SAs regarding more impaired processing speed on the WAIS-III Digit Symbol subtest.

Concerning impulsivity-related behavior, a previous history of self-injurious behavior was found to be associated with a risk of SAs (43,44). The odds ratio ranged from 2.98 to 4.27 and substantially increased to 31.88 when only recent behavior (three months from SAs) was considered. More broadly speaking, a previous history of violent behavior such as “hitting” or “breaking things when angry” was associated with SAs and the odd ratio is 1.43 (47).

Suicide

A Swedish study by Bjorkenstam (55) on the general population found a 4.3 % death rate due to completed suicides among patients with FEP. Moreover, hospitalization for self-injurious behavior without suicide intent prior to FEP diagnosis was associated with an odds ratio of 2.7 for the risk of suicide. Among the suicides in the case control study by De Hert (38) more previous

impulsive behavior was also found (5 times more hospital evasions, twice as many discharges against medical advice, 6 times more aggressive behavior) and a higher IQ. More precisely, patients who died by committing suicide were more likely than controls to have an IQ of over 100 according to an odds ratio of 4.3 (95% CI, 1.7-13).

Concerning the outcome of suicide, no other studies with neuropsychological tests or impulsivity measured by a validated questionnaire were found.

Discussion

This is the first systematic review of the literature concerning the association between neuropsychological or impulsivity measures and suicidal ideation or behavior in patients with FEP. Considering the small number of studies found in the literature, this subject seems to have been little explored to date. Depending on the authors, the inclusion criteria defining patients with FEP vary, leading to much debate about its definition, ranging from patients with an onset of schizophrenia (52) to a much wider inclusion of any patient presenting non toxico-induced psychotic symptoms (55). Selecting only recently-installed schizophrenia cases excludes mood-disordered patients with psychotic symptoms who are at a risk of suicide too, especially near the onset of symptoms. For study purposes, broadening the definition of “first psychotic episode” beyond the diagnosis of recent schizophrenia helps to identify a population at risk including those for whom the diagnosis is uncertain at the time of first contact with the clinician.

Regarding the number of studies included per judgement criterion, only three studies (1,50,54) looked for an association between neuropsychological particularities and the presence of SIs including two which evaluated impulsivity on a dedicated scale (50,54). From a neuropsychological aspect, no particular deficit was found to be significantly associated with SI. But deficits were found to be associated with the likelihood of SAs; and the presence of SI or at least their frequency was strongly associated with this risk (10). This may be explained by the fact that numbers were small with a maximum sample-size of 37 patients with SI (1). However, for

one study (54), less pronounced neuropsychological anomalies were found to be associated with FEP patients and those with SI were more depressed than those without. Faced with the lack of studies with significant concordant results, it has never been possible to conclude on an association so far. Similarly, as regards death by suicide, no studies seeking an association between neuropsychological factors (apart from IQ) or psychological scales measuring impulsivity have been found. As actual suicide is less common than SI or going through with SAs, restrictions in terms of study methodology are far greater. A previous history of impulsive behavior remains strongly associated with the risk of death by suicide in all the studies included.

Only one 2018 study (42) showed a greater impairment in the global score for a battery of neurocognitive tests (performed at the time of first contact for FEP at a psychiatric care unit) in patients with SB. This study was among those with the largest samples included. However no differences were found for most tests in the other study (53) with a similar population (same diagnostic criteria and recruiting mode), and a battery of neuropsychological tests with a follow-up time of over 3 years. In both studies, patients with SI were notably more depressed than those without SI and had a worse premorbid adjustment. Besides, the groups were comparable for the variables under study and there was no statistical adjustment. Only processing speed impairments were found to be separately associated with SAs like the previous study (42). This variation in results raises doubts about the accuracy and reproductibility of neuropsychological tests in this clinical context. Finally, a last study (49) also found deficits in attention, executive functioning and IQ among 152 patients. Only one study (46) found an impairment in theory of mind among suicidal patients. The other studies with fewer patients included and partial neuropsychological evaluations reveal no difference or are contradictory. Thus, neuropsychological anomalies may be found in samples with enough power. Nevertheless, so far these anomalies have always remained too inconsistent in the literature to be used to evaluate the risk of suicide and its prevention in clinical practice. Conversely, self-injurious behavior, even when broadened to include violent

behavior, that could be considered a marker of impulsivity, is systematically found in association with SAs. Such behaviors should alert the clinician to an increased likelihood of suicide.

Limitations

A first limitation is the small number of studies included and, notably, for each outcome: SI, SAs and suicide. Only published studies were included. The hypothesis of a publication bias may be made due to a lack of studies conducted or maybe not published due to inconclusive neuropsychological tests. However, our inclusion criteria were as unrestrictive as possible.

A second limitation is about the studies design. Studies were mainly observational, transversal-type studies with a low level of evidence. Carrying out more case control and cohort studies would lead to results with greater scientific validity for instance. The selection biases for most of the studies were considered as moderate due to the absence of a systematic inclusion of patients or a lack of information on the subject.

Thirdly, the absence of MeSH terms to describe patients with FEP may also have limited the exhaustivity of the search equation. The population of patients with FEP was sought via several keywords that may have had different definitions depending on authors. The population included is thus rather heterogeneous with a more limited comparison of results between studies.

Also, some studies grouped together patients who had attempted to commit suicide and those who had completed suicide under the expression “patients with suicidal behavior” (42,44,48,51) : Now, these two populations may be distinct from a neuropsychological viewpoint. Regarding attempted suicide, some studies consider attempts made after the patient has entered into what turns out to a psychotic disorder (38,42–46), whereas others take into account all attempts (47–52). However the psychopathological mechanism of suicide attempts made during a first episode may have its own neuropsychological particularities.

Finally, there were several limits concerning the evaluation of the outcome. Only four studies had a fairly exhaustive battery of tests which leads to a loss of information. However, using

a variety of neuropsychological tests increases the possibility of finding a chance association (multiple comparisons). Moreover the heterogeneousness of tests and tools used may create a bias in the interpretation of results. Furthermore, most of the studies had to be quoted with a strong bias about doing blind evaluations considering the absence of information on this subject. And yet this bias was probably overestimated. Finally, an adjustment on comorbidities (such as depression) which may alter cognitive functioning, was not made systematically. Nevertheless, the tools for measuring symptoms and suicidal behavior used in the studies mentioned are valid and reliable, limiting classification biases.

Conclusion

There are no arguments arising from this review for an association between neuropsychology and the presence or not of SI among patients with FEP. Evaluations of impulsivity based on psychometric scales do not systematically lead to significant results. The most significant results are related to SAs, rather than SI. According to the majority of studies identified in this article about SAs (especially studies with larger samples), more noticeable cognitive impairment (but only for some tests in the battery) is found associated with SAs among patients with FEP (42,46,51–53). Patients with SAs or who died by suicide were more likely to present aggressive behavior with an impulsive component, and this result was unanimous for all the studies included. New studies, with sufficient power and a consensual definition of FEP, are warranted since the interest of a full neuropsychological battery to identify suicide risk in these patients is still unclear. The use of neuropsychological measures of impulsivity rather than paper-and-pencil tests should be particularly encouraged. Indeed, considering the current development of cognitive remediation techniques, clearly identifying neuropsychological profiles with a higher suicide risk may help to prevent suicidal behavior during early patient management.

In practice, among patients with first episode psychosis, the following points should be considered.

- Non-suicidal self-injurious behavior and impulsive behavior can be associated with the risk of attempted and completed suicide.
- No study has demonstrated an association between cognitive impairments and suicidal ideation.
- Some cognitive impairments, such as a deficit in theory of mind, increase the likelihood of attempted suicide.

Supplementary material

See Appendix.

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Conflicts of interest

There are no conflicts of interest.

Authors' contributions

All authors participated and made substantial contributions to this paper.

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Figure and Tables

Figure 1: Flow chart

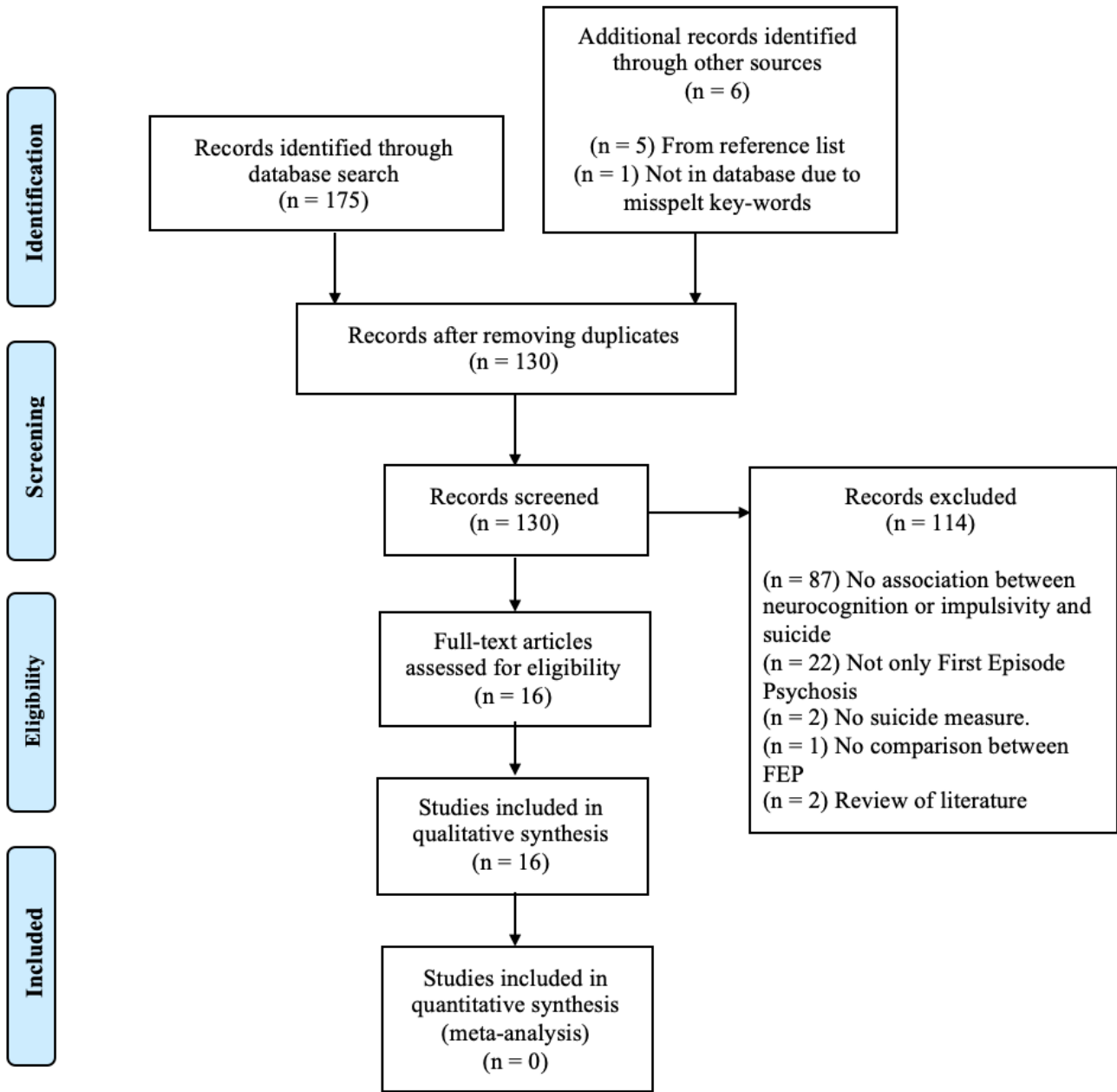


Table 1: Study characteristics

Study	Country	Design	Mean duration of follow-up, years	Sample Size, n	Age, years	Male, %	Population
Cohen et al., 1994 (56)	USA	Transversal	No follow-up	184 patients SA: 61	54% under 30 y.o at inclusion	50%	First admission psychotic patient
De Hert et al., 2001 (38)	Belgium	Case control	11.4	S: 63	22 y.o	61,6%	Young people suffering from schizophrenia
Robinson et al., 2010 (43)	Australia	Cohort	7.4	282 patients SA: 61	21.3 y.o	70.9%	FEP
Fedyszyn et al., 2012 (44)	Australia	Case control	1,5	180 patients SB: 72	19.6 y.o (SD: 2.73)	56.1%	FEP
Huber et al., 2012 (49)	Germany	Transversal	No follow-up	152 inpatients Suicidality at admission: 28	24.5 y.o (SD: 4.9)	74%	FEP
Zhang et al., 2013 (48)	China	Transversal	No follow-up	33 patients High risk group: 14	About 23 y.o	54.4%	First-episode schizophrenic patients
Bjorkenstam et al., 2014 (55)	Sweden	Cohort	Followed until death	2819 patients S: 121	22.6 y.o (SD: 3.6)	58%	FEP
Chang et al., 2014 (1)	China	Transversal	No follow-up	89 patients SI: 37	20.5 y.o (SD: 3.3)	48.3%	FEP
Minzenberg et al., 2014 (50)	USA	Transversal	No follow-up	35 patients SI: 18 SI + SA: 8	21.5 y.o	80%	Recent onset schizophrenia
Ayesa-Arriola et al., 2015 (53)	Spain	Cohort	3	397 patients SA: 60	28.7 y.o (SD: 9.01)	56.9%	First episode non affective psychosis
Minzenberg et al., 2015 (51)	USA	Transversal	No follow-up	17 patients SB: 8	About 24 y.o	64.7%	Recent onset schizophrenia
Canal-Rivero et al., 2017 (46)	Spain	Cohort	1	65 patients SA: 20	26.2 y.o (SD: 9.53)	67,7%	FEP
Canal-Rivero et al., 2018 (42)	Spain	Cohort	3	517 patients SB: 51	29.9 y.o (SD: 9.35)	57.4%	First episode of non affective psychosis
Long et al., 2018 (54)	China	Transversal	No follow-up	63 patients SI: 18	24 y.o	54%	First episode schizophrenia
Zhang et al., 2018 (52)	China	Transversal	No follow-up	357 patients SA: 43	27.6 y.o (SD: 9.4)	48.5%	First-episode and drug naïve patient with schizophrenia
Lopez-Morinigo et al., 2019 (45)	United-Kingdom	Cohort	AESOP: 10 GAP: 5	181 patients; SA: 16 112 patients; SA: 22	30.5 y.o (SD: 1,3) 29.4 y.o (SD: 9.2)	55.8% 65.2%	FEP

FEP: first-episode psychosis. S: suicide. SA: suicide attempt. SB : suicidal behaviour (attempt and suicide). SI : suicidal ideation.
 AESOP: Aetiology and Ethnicity in Schizophrenia and Other Psychoses study. GAP: Genetics and Psychosis study

Table 2: Quality assessment according to the Effective Public Health Practice Project Tool

Study	Selection bias	Study design	Confounders	Blinding	Data Collection Methods	Withdrawals and drop-out	Global Rating
Cohen et al., 1994 (47)	2	3	3	3	1	2	3
De Hert et al., 2001 (38)	2	2	3	3	1	2	3
Robinson et al., 2010 (43)	2	2	3	3	1	2	3
Fedyszyn et al., 2012 (44)	1	2	3	3	1	2	3
Huber et al., 2012 (49)	3	3	3	3	1	2	3
Zhang et al., 2013 (48)	2	3	3	3	1	2	3
Bjorkenstam el al., 2014 (55)	1	2	3	1	1	2	2
Chang et al., 2014 (1)	2	3	3	3	1	2	3
Minzenberg et al., 2014 (50)	2	3	1	3	1	2	3
Ayesa-Arriola et al., 2015 (53)	2	3	3	3	1	3	3
Minzenberg et al., 2015 (51)	2	3	1	3	1	2	3
Canal-Rivero et al., 2017 (46)	2	2	3	3	1	1	3
Canal-Rivero et al., 2018 (42)	2	2	3	3	1	3	3
Long et al., 2018 (54)	2	3	1	3	1	2	3
Zhang et al., 2018 (52)	2	3	3	3	1	2	3
Lopez-Morinigo et al., 2019 (45)	2	2	3	3	1	1	2

Strong: 1. Moderate: 2. Weak: 3

Table 3: Association between neuropsychological measures or impulsivity and suicide among first-episode psychosis patients

Study	Suicide outcome	Neuropsychology or impulsivity outcome	Neuropsychology or impulsivity measures	Association (95% CI ou p-value < 5%)
Cohen et al., 1994 (47)	SA	Impulsivity	History of violence at baseline	OR = 1.43 (1.08-1.89)
De Hert et al., 2001 (38)	S	Impulsivity	Exhibit acting out behavior	OR = 6.4 (2.5-21)
			Discharged against medical advice	OR = 2.5 (1.2-5.8)
			Hospital evasions	OR = 5.6 (2.1-19)
			Involuntary commitment	OR = 17 (2.7-711)
			WAIS IQ over 100	OR = 4.3 (1.7-13)
Robinson et al., 2010 (43)	SA	Impulsivity	History of self-harm at baseline	OR = 4.27 (2.26-8.04)
Fedyszyn et al., 2012 (44)	SB	Impulsivity	Past (three months before cohort entry) non-suicidal, self-injurious behavior	OR = 2.98 (1.29-6.88)
			Recent (three months of the event) non-suicidal self-injurious behavior	OR = 31.88 (6.92-146.76)
Huber et al., 2012 (49)	Suicidality: SI or SA	Processing Speed	TMT-A, Hamburg-Wechsler Adult Intelligence Scale Revised: digit symbol subtest	NS
		Concentration and Attention	d2 test, Testbatterie zur Aufmerksamkeitsprüfung : divided attention and go-nogo	r = - 0.204
		Executive function	Wisconsin Card Sorting Test: completed categories, perseveration errors	r = - 0.184
		Working Memory	Rey Auditory Verbal Learning Test immediate recall, logical memory immediate recall, HAWIE-R digit span test	NS
		Verbal Memory	AVLT delayed recall, logical memory delayed recall	NS
		Verbal Comprehension	HAWIE-R general knowledge and finding similarities	NS
		Logical Reasoning	Leistungsprüfsystem subtest 3, HaWIE-R calculatory reasoning	NS
		Global Cognition	Average of all domains	NS
		General Intelligence	HaWIE-R Intelligence Quotient	r = - 0.212
Zhang et al., 2013 (48)	SB (SSRS)	Working memory	Letter n-back tasking	NS
Bjorkenstam et al., 2014 (55)	S	Impulsivity	Prior hospitalisation for self-harm behaviour	OR = 2.7 (1.7-4.4)
Chang et al., 2014 (1)	SI	Executive function	Modified Wisconsin Card Sorting Test: Categories completed	NS
			Perseverative errors	NS
		Executive function and impulsivity	Hayline Sentence Completion Test part B: total error score	NS
		Impulsivity	Barratt Impulsiveness Scale: Attentional impulsivity	OR = 1.32 (no confidence interval)
			Motor impulsivity	NS
			Non-planning impulsivity	NS
Minzenberg et al., 2014 (50)	SI	Attention and impulsivity	Continuous Performance Task (accuracy and reaction time)	NS
		Impulsivity	Barratt Impulsiveness Scale	NS
	SI + SA	Attention and impulsivity	Continuous Performance Task (accuracy and reaction time)	NS
		Impulsivity	Barratt Impulsiveness Scale	NS
Ayasa-Arriola et al., 2015 (53)	SA	Verbal memory	Rey Auditory Verbal Learning Test (RAVLT) delayed recall	NS
		Visual memory	Rey Complex Figure (RCF) delayed reproduction	NS
		Executive functioning	Trail Making Test (TMT), time to complete TMT-B minus TMT-A	NS
		Working memory	WAIS-III Backward Digits scale (total subscore)	NS
		Processing speed	WAIS-III Digit Symbol subtest, standard total score	t-test: 2005
		Motor dexterity	Grooved Pegboard Handedness, time to complete with dominant hand	NS
		Attention	Continuous Performance Test, total number of correct responses	NS
Minzenberg et al., 2015 (51)	SB	Premorbid IQ	WAIS-III Vocabulary subtest, standard total score.	NS
		Attention	Stroop Task Performance	Superior reaction time for SB
		Impulsivity	Barratt Impulsiveness Scale	NS
Canal-Rivero et al., 2017 (46)	SA	Theory of mind	First-order false belief task	OR = 4.26 (1.05-17.31); X ² = 3.95
			Second-order false belief task	X ² = 6.27
			Hinting task	NS
Canal-Rivero et al., 2018 (42)	SB	Verbal memory	Rey Auditory Verbal Learning Test (RAVLT) delayed recall	NS
		Visual memory	Rey Complex Figure (RCF) delayed reproduction	NS
		Executive functioning	Trail Making Test (TMT), time to complete TMT-B minus TMT-A	NS
		Working memory	WAIS-III Backward Digits scale (total subscore)	NS
		Processing speed	WAIS-III Digit Symbol subtest, standard total score	Effect size: 0.35
		Motor dexterity	Grooved Pegboard Handedness, time to complete with dominant hand	Effect size: 0.5
		Attention	Continuous Performance Test, total number of correct responses	NS
		Premorbid IQ	WAIS-III Vocabulary subtest, standard total score.	NS
		Global Cognitive Functioning	Deviation of the patient from the control in each domain	Effect size: 0.58
Long et al., 2018 (54)	SI	Working Memory	Letter 2-back task target accuracy	F = 11,70
			Letter 2-back task target reaction-time	F = 3,785
			Letter 2-back task non-target accuracy	NS
			Letter 2-back task non-target reaction-time	NS
		Verbal Comprehension	Information Symbol subtest of WAIS-CR	F = 7,271
Zhang et al., 2018 (52)	SA	Processing Speed	Digit Symbol subtest of WAIS-CR	F = 38,219
		Immediate Memory	List Learning and Story Memory tasks	NS
		Visuospatial/Constructional	Figure Copy and Line Orientation tasks	NS
		Language	Picture Naming and Semantic Fluency tasks	NS
		Attention	Digit Span and Coding tasks	F = 5,12
		Delayed Memory	List Recall, Story Recall, Figure Recall, and List Recognition tasks	NS
Lopez-Morinigo et al., 2019 (45)	SA	Premorbid IQ	National Adult Reading Test	AESOP: NS; GAP: NS
		Executive function	Trail Making Test A and B	AESOP: HR = 1.01 (1.00-1.02); GAP: NS

S: Suicide. SA: Suicide Attempt. SB : Suicidal Behaviour (attempt and suicide). SI : Suicidal Ideation.
 F: ANOVA test F. HR: Hazard Ratio. OR: Odd Ratio. NS: Non-Significant. r: Pearson's r. X²: Chi-square
 AESOP: Aetiology and Ethnicity in Schizophrenia and Other Psychoses study. GAP: Genetics and Psychosis study
 SSRS : Schizophrenia Suicide Risk Scale

Appendix

Inclusion criteria concerning first-episode psychosis definition

Study	First-episode psychosis patients included
Cohen et al., 1994 (47)	Age 15-60, evidence of psychosis (presence of any psychotic symptom or grossly disorganized behavior) and first psychiatric hospitalization or not more than 6 months prior to actual admission.
De Hert et al., 2001 (38)	Under 30 years of age at index admission and diagnosis of schizophrenia or schizo-affective disorder
Robinson et al., 2010 (43)	First treated episode of psychosis less than 6 months prior to neuroleptic medication (DSM-III-R and from 1995 DSM-IV diagnosis of a psychotic disorder)
Fedyszyn et al., 2012 (44)	Age 15-24, presence of delusions, hallucinations, disorganized behavior and/or formal thought disorder, and no prior treatment with antipsychotic medication
Huber et al., 2012 (49)	International Classification of Diseases, 10th revision. No detailed definition.
Zhang et al., 2013 (48)	Age 18-45, met DSM IV criteria for schizophrenia, total course of disease < 18 months
Bjorkenstam et al., 2014 (55)	All patients with first hospital-treated psychosis (schizophrenia and schizoaffective disorder, bipolar disorder, depressive disorder with psychotic symptoms, persistent delusional disorder, psychotic disorder due to substance use, acute and transient psychotic disorder and other psychoses) from age 15 to 30 years
Chang et al., 2014 (1)	Age 15-25, first-episode DSM IV schizophrenia, schizophreniform disorder, delusional disorder, brief psychotic disorder, psychosis not otherwise specified
Minzenberg et al., 2014 (50)	Age 18-50, onset of psychotic symptoms within 2 years of study, diagnosis of 295.X by DSM-IV-TR
Ayesa-Arriola et al., 2015 (53)	Age 15-60, no prior antipsychotic medication or less than 6 months, DSM-IV criteria for brief psychotic disorder, schizophreniform disorder, schizophrenia or schizoaffective disorder
Minzenberg et al., 2015 (51)	Age 18-50, diagnosis of schizophrenia with less than 2 years of since onset of overt psychotic illness
Canal-Rivero et al., 2017 (46)	Age 14-54, with at least one symptom (between hallucination, delusions, disorganized speech, catatonia or disorganized behavior and negative symptoms) and first contact with mental health service for psychotic symptoms
Canal-Rivero et al., 2018 (42)	Age 16-60 years, no prior antipsychotic treatment or less than 6 weeks and fulfilled DSM-IV criteria for: schizophrenia, or brief psychotic disorder, or not otherwise specified psychosis, or schizophreniform disorder, or schizoaffective disorder, or delusional disorder
Long et al., 2018 (54)	Diagnosed with schizophrenia in the past 18 months without any previous episode of psychosis using the Structured Clinical Interview for DSM-IV Axis I Disorders, Patient Edition
Zhang et al., 2018 (52)	Age 18-45, acute episode that met DSM IV criteria for schizophrenia, duration of symptoms was no longer than 60 months at admission, no prior antipsychotic treatment
Lopez-Morinigo et al., 2019 (45)	All incident FEP among F10-F29 and F30-F33 ICD-10 codes

DSM: Diagnostic and Statistical Manual of Mental Disorders. FEP: first-episode psychosis.

Search terms used

PubMed: (neuropsych OR mental processes OR cogniti* OR impulsiv*) AND suicid* AND ("first episode psychosis" OR "first episode schizophrenia" OR "recent onset schizophrenia" OR "recent onset psychosis"): 51 articles found and 10 articles included in the study for the narrative summary

Web of science: (neuropsych OR mental processes OR cogniti* OR impulsiv*) AND suicid* AND ("first episode psychosis" OR "first episode schizophrenia" OR "recent onset schizophrenia" OR "recent onset psychosis") all fields: 76 articles with no new articles to include

*Science direct: (neuropsychology AND suicide AND "first episode psychosis"): 70 results and 20 articles with no new articles to include

*Pascal et Francis: (neuropsychology AND suicide AND first episode psychosis): 14 articles and no new articles to include

*Academic Search Premier: (neuropsychology or neuropsychological AND suicidal ideation or suicidal behavior or suicidal thoughts or suicide attempt or suicidality AND first episode psychosis): 9 articles and no new articles to include

*PsycInfo: (neuropsychology or neuropsychological AND suicidal ideation or suicidal behavior or suicidal thoughts or suicide attempt or suicidality AND first episode psychosis): 4 articles with no new articles to include

*PubPsych: (neuropsychology or neuropsychological) AND (suicidal ideation or suicidal behavior or suicidal thoughts or suicide attempt or suicidality) AND (first episode psychosis): 1 article and no new articles to include

*PsycArticles: (neuropsychology or neuropsychological AND suicidal ideation or suicidal behavior or suicidal thoughts or suicide attempt or suicidality AND first episode psychosis): no articles

*Base santé psy : (neuropsychologie ET suicide ET premier épisode psychotique) : no articles

*Cochrane Library : no articles

Serment d'Hippocrate

En présence des Maîtres de cette école, de mes chers condisciples et devant l'effigie d'Hippocrate, je promets et je jure, au nom de l'Être suprême, d'être fidèle aux lois de l'honneur et de la probité dans l'exercice de la médecine.

Je donnerai mes soins gratuits à l'indigent et n'exigerai jamais un salaire au-dessus de mon travail.

Admis dans l'intérieur des maisons, mes yeux ne verront pas ce qui s'y passe, ma langue taira les secrets qui me seront confiés, et mon état ne servira pas à corrompre les mœurs, ni à favoriser le crime.

Respectueux et reconnaissant envers mes Maîtres, je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.

Que les hommes m'accordent leur estime si je suis fidèle à mes promesses. Que je sois couvert d'opprobre et méprisé de mes confrères si j'y manque.

Résumé

Contexte: La prévalence des idées et comportements suicidaires parmi les patients souffrant de trouble psychotique est un problème majeur de santé publique. La majorité des tentatives de suicide surviennent avant ou près de l'entrée dans un premier épisode psychotique (PEP). Approfondir les connaissances sur le risque suicidaire dans les premiers stades de la maladie est essentiel pour développer des stratégies thérapeutiques et préventives. Nous avons réalisé une revue systématique de la littérature pour investiguer une association entre déficits neurocognitifs ou des antécédents de comportements impulsifs avec la présence d'idées ou comportements suicidaires chez les patients souffrant d'un PEP.

Méthode: Les recommandations PRISMA ont été suivies. Dix bases de données ont été interrogées notamment via PubMed, utilisant les termes MeSH ou mots-clés relatifs au PEP, à l'impulsivité ou des mesures de fonctions cognitives, et la présence d'idées ou comportements suicidaires.

Résultats: Seize études ont été incluses. Cinq études montrent des déficits neuropsychologiques plus prononcés notamment sur le plan attentionnel, de la vitesse de traitement, des fonctions exécutives et de la théorie de l'esprit chez des patients souffrant d'un PEP réalisant des tentatives de suicide. A ce jour, aucune étude n'a montré d'association entre un déficit cognitif objectivé sur un test neuropsychologique et la présence d'idées suicidaires. Les antécédents de comportements impulsifs non suicidaires sont retrouvés associés aux tentatives de suicide et suicides aboutis.

Conclusion: D'autres études neuropsychologiques sont nécessaires pour identifier les mécanismes reliant ces anomalies neuropsychologiques aux conduites suicidaires et évaluer l'utilité en tant que cible thérapeutique.

Mots-clés: Trouble psychotique, Premier épisode psychotique, Neuropsychologie, Impulsivité, Idées suicidaires, Tentatives de suicide, Suicide