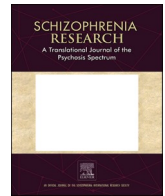




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Distribution and frequency of clinical criteria and rating scales for diagnosis and assessment of catatonia in different study types

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ABSTRACT

Background: A comprehensive assessment of catatonic symptoms is decisive for diagnosis, neuronal correlates, and evaluation of treatment response and prognosis of catatonia. Studies conducted so far used different cut-off criteria and clinical rating scales to assess catatonia. Therefore, the main aim of this study was to examine the frequency and distribution of diagnostic criteria and clinical rating scales for assessing catatonia that were used in scientific studies so far.

Methods: We conducted a systematic review using PubMed searching for articles using catatonia rating scales/criteria published from January 1st 1952 (introduction of catatonic schizophrenia to first edition of the Diagnostic and Statistical Manual of Mental Disorders [DSM]) up to December 5th, 2022.

Results: 1928 articles were considered for analysis. 1762 (91,39 %) studies used one and 166 (8,61 %) used ≥ 2 definitions of catatonia. However, 979 (50,7 %) articles did not report any systematic assessment of catatonia. As for clinical criteria, DSM criteria were used by the majority of studies ($n = 290$; 14.0 %), followed by International Classification of Diseases (ICD) criteria ($n = 61$; 2.9 %). The Bush-Francis Catatonia Rating Scale (BFCRS) was found to be by far the most frequently utilized scale ($n = 464$; 22.4 % in the respective years), followed by Northhoff Catatonia Rating Scale (NCRS) ($n = 31$; 1.5 % in the respective years).

Conclusion: DSM and ICD criteria as well as BFCRS and NCRS were most frequently utilized and can therefore be recommended as valid instruments for the assessment of catatonia symptomatology.

1. Introduction

In both neuroscience and clinical research, catatonia rating scales are important for patients' screening, inclusion or exclusion, stratification and determination of outcome endpoints. Furthermore, a better understanding of the pathophysiology and pharmacology of catatonia will inevitably depend on precise assessment of catatonia severity and symptom variations. After the introduction of the diagnosis "schizophrenic reaction, catatonic type" in the first edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM) in 1952, there was an increase in the number of cohort and case studies on catatonia (for review see Cattarinussi et al., 2022; Hirjak et al., 2020 and Walther et al., 2019). However, these studies have relied on different number of affective, motor and behavioral psychomotor features and used

heterogeneous cut-off criteria as well as clinical rating scales to define catatonia. The use of different definitions and criteria of catatonia led to different prevalence, neurobiological correlates and unfortunately to different conclusions, depending on the criteria or scale used (Hirjak et al., 2020).

From a clinical perspective, the symptoms of catatonia are complex and therefore, clinical and neuroscientific research into catatonia depends on the reliable and accurate measurement of the affective, motor and behavioral catatonic symptoms (Hirjak et al., 2022c). In particular, catatonia often needs to be distinguished from other disorders such as malignant neuroleptic syndrome (MNS) or parkinsonism. Further, other clinical and environmental factors need to be considered and therefore clinical judgement of an experienced clinician is often required.

Although many clinical criteria and rating scales are currently

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known and used in different types of studies on catatonia, the frequency and distribution of different catatonia definitions that have been used in the published literature have not been studied, yet. Therefore, this systematic review has three main objectives: First, we will systematically review which clinical/operationalized criteria and which clinical rating scales have been used to define and assess catatonia over the last 70 years. Second, we will also examine their frequency and distribution among the systematically identified case reports, clinical and observational studies. Third, we will present the most commonly used clinical criteria and rating scales and discuss why these instruments in particular have been used most often in scientific studies on catatonia. In this context, we will also discuss the contribution of such clinical criteria and rating scales to the definition of catatonia in general.

2. Methods

2.1. Search strategy and study selection

The search strategy and study selection followed PRISMA guidelines. The literature was searched using MEDLINE (source PubMed, January 1, 1952 to December 5th, 2022), and by additional hand searches through reference lists and specialist psychiatric and neuroscience journals. The main goal was to identify studies reporting cut-off criteria and clinical rating scales to assess catatonic symptoms. The following search terms or their combinations were used: “catatonia”, “catatonic symptoms”, and “catatonic syndrome”. The automatic search was completed by cross-checking the reference lists of the identified studies and of previous systematic reviews on this topic. We also searched for articles published in any language and scrutinized references from these studies to identify other relevant studies. There were no language restrictions with respect to publication date or country of origin within the first search run, although the majority of ultimately extracted articles were in English or German. We did not consider unpublished studies, conference abstracts

or poster presentations. Each identified article was examined for sets of clinical criteria, references to diagnostic manuals (DSM or ICD) and clinical rating scales defining catatonia.

2.2. Study selection and eligibility criteria

We imposed the following methodological restrictions for the inclusion criteria: (a) Clinical and neuroimaging cohort and case studies that investigated catatonia in mental disorders; (b) Clinical and neuroimaging cohort and case studies that were reported in an original article in a peer-reviewed journal. We only included articles in English and German. Cohort and case studies reporting catatonia in manifest neurological (including oncological) disorders were excluded. We also excluded reviews, letters to the editor without case reports, commentaries, animal studies and post-mortem studies. Studies considered of interest were reviewed and cross-checked independently by two authors (GAB and DH). In case of multiple publications, the most up to-date or comprehensive information was used. A similar approach has been used previously in systematic reviews on schizophrenia spectrum disorders (SSD) and other mental disorders (Baum et al., 2015; Ewers et al., 2011; Hirjak et al., 2018; Naismith et al., 2012).

3. Results

A PubMed search on December 5th 2022 yielded 4319 hits since January 1st 1952. Based on the screening of the 3658 titles and abstracts, we identified 1928 articles that mentioned sets of criteria and clinical rating scales for catatonia (see Fig. 1 - PRISMA flow-chart for details). In particular, we closely examined 1337 case reports, 526 clinical and 65 observational studies that included neuroimaging (structural and functional magnetic resonance imaging (MRI) and Single Photon Emission Computed Tomography (SPECT)), neurophysiological assessments (e.g. EEG-studies) and other study types (GWAS and

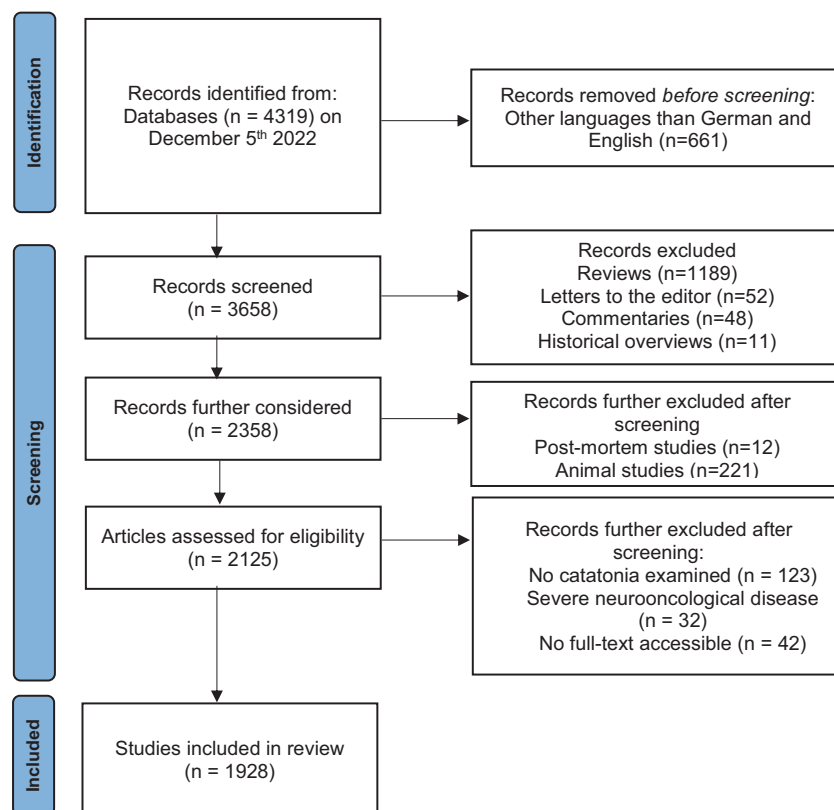


Fig. 1. PRISMA flow-chart.

biocompatible material). Of 1928 articles closely examined, 783 articles mentioned 1 set of clinical criteria or clinical rating scale. 166 articles mentioned ≥ 2 sets of clinical criteria or ≥ 2 clinical rating scales or their combination. In 979 articles no systematic assessment of catatonic symptoms was reported. We consider it important to also include studies that used ≥ 2 sets of clinical criteria or clinical rating scales in the analysis because we wanted to present a more realistic distribution of catatonia definitions. However, no full texts were available for 42 articles and we did not receive any response from the corresponding author either. [Table 1](#) presents the frequency and distribution of different sets of criteria and clinical rating scales used within different study types and identified during the review process.

4. Discussion

This systematic review provides an update on the distribution and frequency of clinical criteria and clinical scales that have been used to define and assess catatonia in different types of scientific studies. Three main findings emerged: (i) This systematic review found that despite the availability of clinical criteria and clinical rating scales, only half of the studies used an established instrument to define catatonia. (ii) As might be expected, before clinical scales were developed and validated, it was typical to assess catatonia solely based on clinical presentation, including specific criteria, as e.g. referred to in DSM or ICD. The frequency in these assessment scales was similar across the years, except for a numerical rise in usage of the clinical rating scales in late 1990s. (iii)

After the introduction of BFCRS in 1996 and NCRS in 1999, the vast majority of studies used these clinical rating scales to diagnose catatonia. The BFCRS (23 items) was by far the most commonly used clinical rating scale for catatonia. It was followed by the NCRS (40-item version), which has been used frequently in MRI studies, especially in the last 5 years ([Hirjak et al., 2021](#); [Cattarinussi et al., 2022](#)).

First, it is somehow surprising that the majority of studies did not report how catatonia was diagnosed. In the last 150 years, clinicians and researchers have been trying to assess psychopathological symptoms according to objective, valid and reliable criteria. Clinical ratings scales were mainly used for this purpose, even though in recent years, there has also been an increase in the use of electronic assessments (e.g. actigraphy and smartphone-based ecological momentary assessment) to monitor psychopathological symptoms (including catatonia ([von Kanel et al., 2022](#); [Walther et al., 2022](#))) in scientific studies. However, despite these efforts, catatonia is still poorly known, often misunderstood and underdiagnosed among psychiatrists ([Cooper and Roig Llesuy, 2017](#); [Llesuy et al., 2018](#); [Takacs et al., 2021](#)). A recent study ([Wortzel et al., 2021](#)) used an online 50-item multiple-choice test and 3-min standardized patient video to be scored using the BFCRS to examine theoretical and clinical knowledge on catatonia in a sample of 482 medical students, psychiatry residents or fellows, and psychiatrists. The authors found that there was a discrepancy between theoretical and practical knowledge. In particular, multiple items of the BFCRS were poorly understood (e.g. mannerisms, Gegenhalten, perseveration, verbigeration, and waxy flexibility) and some of them were not assessed correctly (e.g.

Table 1

Distribution and frequency of study types using different clinical criteria and rating scales for the diagnosis and assessment of catatonia.

	Case reports	Clinical studies	Observational studies ^a	Frequency	Percentage
Clinical criteria set					
DSM (total)	129	148	13	290	14.1 %
1st edition	0	0	0	0	0 %
2nd edition	1	6	0	7	0.3 %
3rd edition	11	45	2	58	2.8 %
4th edition	109	89	9	207	10.1 %
5th edition	8	8	2	18	0.9 %
ICD (total)	16	45	0	61	3.0 %
8th edition	2	5	0	7	0.3 %
9th edition	3	19	0	22	1.1 %
10th edition	11	20	0	31	1.5 %
11th edition	0	1	0	1	0.05 %
Clinical rating scale					
BFCRS	336	119	9	464	22.6 %
NCRS	7	11	13	31	1.5 %
BFCSI ^b	6	22	2	30	1.5 %
Lorazepam-Test	25	0	0	25	1.2 %
MRS	2	18	2	22	1.1 %
Rosebush et al., 1990	9	13	0	22	1.1 %
Lohr and Wisniewski, 1987	6	12	0	18	0.9 %
BCRS	4	10	0	14	0.7 %
Kanner-Scale	8	1	0	9	0.4 %
Amytal-Interview	6	1	0	7	0.3 %
PCRS	3	3	0	6	0.3 %
RCS	3	2	0	5	0.2 %
CASH-Criteria	0	5	0	5	0.2 %
Zolpidem-Test	4	0	0	4	0.2 %
ABQ	0	2	0	2	0.1 %
Residual category ^c	18	38	0	56	2.7 %
No systematic assessment	817 (58.4)	130 (22.4 %)	33 (45.8)	979	47.7 %
Total	1399 (68.2 %)	580 (28.3 %)	72 (3.5 %)	2051	100 %

Abbreviations: ABQ = Attenuated Behavior Questionnaire; BCRS = Bräunig Catatonia Rating Scale; BFCRS = Bush Francis Catatonia Rating Scale; CASH-Criteria = Comprehensive Assessment of Symptoms and History; DSM = Diagnostic and Statistical Manual of Mental Disorders; ICD = International Statistical Classification of Diseases and Related Health Problems; MRS = Modified Rogers Scale; NCRS=Northoff Catatonia Rating Scale; PCRS = Pediatric Catatonia Rating Scale; RCS = Rogers Catatonia Scale.

^a The category "observational studies" includes neuroimaging, physiological and genetic studies examining catatonia.

^b BFCSI = 14-item screening of BFCRS.

^c e.g. unsystematically set criteria of [Leonhard \(1979\)](#); [Gjessing \(1932\)](#); [Kahlbaum \(1874\)](#); psychomotor symptoms derived from AMDP; AMDP = Manual zur Dokumentation psychiatrischer Befunde, Editor. Arbeitsgemeinschaft für Methodik und Dokumentation in der Psychiatrie.

combativeness, echopraxia/echolalia, negativism, posturing/cataplexy, rigidity, withdrawal). They recommended standardization of catatonic assessment and greater education of clinicians on catatonia (Wortzel et al., 2021).

Second, until 1991 and the introduction of the Modified Rogers Scale (MRS) by Lund et al. (1991) and McKenna et al. (1991), no standardized clinical rating scales were available to systematically assess catatonia (for historical milestones see Fig. 2). Clinicians therefore assessed catatonia according to different sets of diagnostic criteria such as those mentioned in DSM or ICD as well as in publications by Gjessing (1932), Leonhard (1979), Barnes et al. (1986), Lohr and Wisniewski (1987) and Rosebush et al. (1990) (for detailed analysis of the clinical criteria see also (Oldham, 2022)). All these references provide a list of different catatonia symptoms and suggested that any two signs are sufficient to diagnose catatonia (Fink, 1994). The DSM and ICD manuals initially included catatonia as a subtype of schizophrenia. It was not until the 1980s that catatonia was also associated with other psychiatric disorders (Fink, 1994, 2011). In 1993, besides catatonic schizophrenia (F20.2), ICD-10 mentioned a new diagnosis “organic catatonic disorder” (F06.1) for the first time (Dilling et al., 1994). In 1994, the DSM-IV manual made it possible to also diagnose catatonia associated with medical illnesses (Catatonic Disorder due to a General Medical Condition) and affective disorders (Episode Specifier for Major Mood Disorders) (Fink, 1994). However, ICD and DSM systems mentioned only few catatonic symptoms and have cut-off criteria which vary between 2 and 3. Also, clinical rating scales for ICD and DSM with detailed description of individual catatonic symptoms are currently not available.

Third, the BFCRS has been used most frequently among clinicians and scientists. This is not surprising and we would like to list and discuss some of the reasons for this here: First, BFCRS is the most frequently cited scale in the entire scientific literature on catatonia (Weleff et al., 2022). Second, BFCRS mainly maps motor and behavioral symptoms. This is in line with Emil Kraepelin and Eugen Bleuler's concept of catatonia as a motor disorder and a subtype of schizophrenia, which has been adopted in Psychiatry for >120 years (Hirjak et al., 2022a; Hirjak et al., 2022b). Third, there is a comprehensive online teaching material on how to rate the individual items of the BFCRS (see also <https://www.urmc.rochester.edu/psychiatry/divisions/collaborative-care-and-wellness/bush-francis-catatonia-rating-scale.aspx>) (Wortzel et al., 2022). An online version with detailed instructions and videos not only makes the scale more visible, but also easier to comprehend for psychiatrists. The second most common scale is the NCRS. Northoff et al. (1999) designed this scale following modern and historical literature and therefore included a number of affective symptoms. The NCRS contains a total of 40 symptoms which are divided into three dimensions, e.g. affective, motor and behavioral. Patients with catatonia must exhibit at least 1 symptom in all three domains to be diagnosed as catatonic. Unlike the BFCRS and all other catatonia scales (Sienaert et al., 2011), the NCRS includes 13 affective symptoms, thus reflecting the truly psychomotor

concept of Kahlbaum (Hirjak et al., 2022a; Kahlbaum, 1874). The three symptom domains of the NCRS reflect also the syndrome character of catatonia as it can be associated with both psychotic and mood disorders. The inclusion of the affective domain marks catatonia as truly psychomotor disorder rather than as motor disorders as it seems to be implied by the BFCRS (see also (Hirjak et al., 2020; Northoff et al., 2021)). More precisely, clinical rating scales for catatonia, with very few exceptions (e.g. NCRS), emphasize motor signs and assess very few, if any, affective symptoms. Further, in our opinion, the BFCRS mentions only motor symptoms. Combativeness (“Belligerence or aggression, usually in an undirected manner, without explanation”) may be broadly understood as an affective symptom, at least in some circumstances. However, from our point of view, the other symptoms of the BFCRS are motor-behavioral symptoms. Hence, BFCRS and NCRS conceive catatonia as either motor or psychomotor which is well reflected in the included items and domains (Hirjak et al., 2022b). In line with this, the different compilation of catatonic symptoms within the BFCRS and NCRS has led to different neural correlates of catatonia, i.e. depending on the scale used (see (Hirjak et al., 2020) for further details). Finally, the BFCRS, along with the DSM and ICD, are instruments highlighting the motor-behavioral concept of catatonia, the NCRS supports the truly psychomotor character of catatonia by also considering affective symptoms and other for catatonia relevant behavioral symptoms.

This review has implications for researchers and practitioners interested in examining catatonia. In determining the optimal ways to assess catatonia in daily clinical routine and scientific studies, multiple methodological issues need to be considered. The first relates to the question whether catatonia is conceptualized as a separate (stand-alone) diagnostic entity or as an additional description of other psychiatric illnesses (in terms of a specifier). A second and related methodological issue is the theoretical basis of catatonia symptomatology. In recent years, two predominant concepts of catatonia have become established (Hirjak et al., 2022a; Hirjak et al., 2022b): The first, stemming more from the tradition of Kraepelin (Kraepelin, 1899) and Bleuler (Bleuler, 1911), with a strong focus on motor symptoms and their neural correlates in the dopamine-associated sensorimotor system (Walther et al., 2019). The second concept, stemming more from the tradition of Kahlbaum (1874), with a truly psychomotor focus and neural correlates in GABA, glutamate- and serotonin-associated networks (Hirjak et al., 2020; Northoff et al., 2021). When examining (rating) and diagnosing catatonic symptoms, it is important to have both concepts in mind in order to avoid misdiagnosis and/or underrecognition of this condition.

Although national and international treatment guidelines for SSD (e.g., by the American Psychiatric Association (APA), National Institute for Health and Care Excellence (NICE), World Federation of Societies of Biological Psychiatry (WFSBP), British Association of Psychopharmacology (BAP), or German Society for Psychiatry und Psychotherapy, and Psychosomatic (DGPPN)) include recommendations for the treatment of acute catatonia, there are no recommendations for potential benefits of

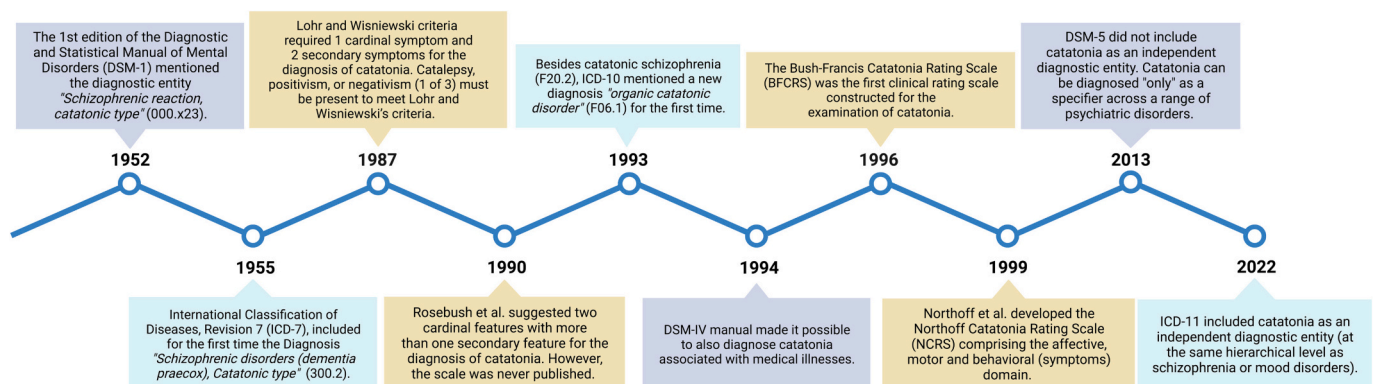


Fig. 2. Important milestones in the history of catatonia concept and diagnostic criteria.

post-catatonc psychotherapeutic treatment as a tertiary prevention strategy. To date, recommendations for non-pharmacological treatment (e.g. psychotherapeutic interventions) of post-catatonc patients is still rare (Zingela et al., 2022). Many of the post-catatonc patients suffer from affect lability, irritability, insecurity, and anxiety, even beyond the acute phase. Many of them are very sensible, emotional and vulnerable individuals, who have great difficulties to process negative external stimuli. Furthermore, in the defined time period (1952–2022), we identified only few studies on the subjective experience of catatonc patients (Dell'Osso et al., 2022; Northoff et al., 1996; Rosebush and Mazurek, 2010; Zingela et al., 2022). In particular, two questionnaires were developed to assess (a) subjective experience of catatonc patients (Northoff et al., 1996) and (b) to explore the symptomatology of the catatonc spectrum across the lifespan (Dell'Osso et al., 2022). In the future, if these questionnaires find their way into clinical routine, the subjective information regarding the patients' symptoms could accompany the therapeutic process in the post-acute phase and improve the tertiary prevention of catatonc.

Finally, after the introduction of catatonc in ICD-11, there seems to be a growing interest in the subjective experience of catatonc patients (Dawkins et al., 2022; Zingela et al., 2022). From a clinical and scientific point of view, it is also important to systematically examine the subjective experience of catatonc patients, e.g. in order to develop new endpoints for clinical trials and disorder-specific psychotherapeutic interventions. Last but not least, whether one uses BFCRS or NCRS, catatonc can be defined by >1000 different symptom constellations (Dawkins et al., 2022). In the future, it will be important to examine the prevalence of different catatonc symptoms and define core symptoms in order to reduce the number of possible symptom constellations leading to the diagnosis of catatonc. For this purpose, we strongly acknowledge large and deeply phenotyped cohorts of catatonc patients who have been examined with different sets of clinical criteria (e.g. DSM and ICD) and clinical rating scales (e.g. BFCRS and NCRS).

4.1. Limitations

This study has the following limitations: (1) We only focused on the last 70 years and therefore we may not have identified all the studies on catatonc. However, by January 1st 1952, only 41 hits were obtained under the above mentioned search criteria. Further, it was challenging to determine the exact time period for the systematic analysis. In this context, a significant question may arise as to why 1952 was chosen as a starting point, because the first edition of DSM published in 1952 does not offer operationalized criteria of catatonc. The first edition of DSM describes “Schizophrenic reaction, catatonc type” (000.x23) as “These reactions are characterized by conspicuous motor behavior, exhibiting either marked generalized inhibition (stupor, mutism, negativism and waxy flexibility) or excessive motor activity and excitement. The individual may regress to a state of vegetation.” (see p. 26). Although this definition mentions some catatonc symptoms, it was not until the DSM III that operationalized criteria for catatonc were included. The third edition of DSM thus represented a revolution in the previous classification because of the operationalized criteria for psychiatric disorders. Other innovations were the multiaxial classification and the extensive detachment from cause- and theory-related terminology. The DSM III was therefore considered a “paradigm shift” and triggered a massive increase in research efforts in psychiatry. However, the aim of this study was not to examine the different operationalized criteria of catatonc (for a comparative phenotypic analysis see (Oldham, 2022)), but rather the frequency and distribution of different catatonc definitions in case, clinical and observational (inkl. neuroimaging) studies. (2) We only performed a PubMed search and did not use other databases such as Cochrane Library, Google Scholar, Ovid Embase, Ovid MEDLINE, Scopus, and Web of Science Core Collection. PubMed is free, easy to use, contains early online articles, is updated daily, thus allowing a comprehensive follow-up of a specific topic (Falagas et al., 2008). Still,

although it is very unlikely, it is possible that we have missed some studies and case reports on catatonc. (3) It may also be that the Modified Rogers Scale (MRS) did not identify some studies because the MRS captures extrapyramidal motor symptoms as well as catatonc. Nevertheless, we assume that the apparent distribution and frequency of criteria and clinical scales would not change significantly. (4) Although half of the identified publications failed to use diagnostic criteria, this result may be biased by different factors. After the identified articles were divided into case, clinical, and observational studies (see Table 1), it became evident that more than half (58.4 %) of the case reports, but only about one-fourth (22.4 %) of the clinical trials mentioned an exact definition of catatonc. Therefore, we might speculate that clinical studies/trials are far more likely to use diagnostic criteria or rating scales than case reports or case series. However, numbers of participants within the different study types were not considered by the present review. Therefore, the missing association between (a) the use of operationalized criteria and (b) size of the study might be considered a possible limitation of the present study. Still, there is a temporal gradient in the use of operationalized criteria. (5) We excluded studies involving severe neuro-oncological disorders and focused primarily on catatonc associated with psychiatric and medical conditions. The reason for this decision was that patients with different neuro-oncological diseases may show different psychomotor symptoms depending on which brain areas are affected, leading to biased conclusions regarding pathophysiology of catatonc. (6) Finally, since we also included studies on patients with malignant neuroleptic syndrome and catatonc symptoms, it is not possible to distinguish between the frequency of catatonc criteria and rating scales in the context of genuine catatonc symptomatology and antipsychotic-induced catatonc.

5. Conclusion

DSM and ICD criteria as well as BFCRS and NCRS are valid criteria/instruments, were most frequently utilised and can therefore be recommended for the assessment of catatonc. Although the examination of catatonc symptoms using instrumental assessments in daily clinical routine and scientific studies is still rare, we consider the development of such objective and reliable markers as essential since we believe that it will beneficially complement the experienced clinician's judgement and expertise as well as greatly improve understanding and ratings of less experienced clinicians and researchers.

CRediT authorship contribution statement

DH and RCW: original idea and design of the review. DH and RCW: first draft of the manuscript. DH and GAB: systematic literature search. DH, GAB, and KMK: interpretation of findings. DH, GAB, SF, KMK, GN and RCW: discussion of the results, writing and manuscript revision.

Role of the funding source

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Declaration of competing interest

The authors have declared that there are no conflicts of interest in relation to the subject of this study.

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Fig. 2 was created by BioRender.com.

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