Movement Disorders in Adults With Intellectual Disability and Behavioral Problems Associated With Use of Antipsychotics

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Background: Antipsychotic drugs are prescribed to approximately 30% to 40% of adults with intellectual disability (ID) and behavioral problems despite lack of evidence of effectiveness and potential adverse effects, including movement disorders.

Aims: The aim of this study was to examine the prevalence of movement disorders (dyskinesia, akathisia, dystonia, and parkinsonism) in in-patient adults with mild to borderline ID and behavioral problems associated with use of antipsychotics.

Methods: Prevalence of movement disorders was measured with a standardized protocol. The strength of the association between antipsychotic drug use and movement disorders was assessed using logistic regression analysis.

Results: Almost half (44.0%) of 134 in-patient adults with ID and behavioral problems had any movement disorder. Parkinsonism, dyskinesia, akathisia, and dystonia were present in, respectively, 36.6%, 11.2%, 9.0%, and 0.7% of patients with ID. It appeared that current use of any antipsychotic drug (odds ratio, 3.0; 95% confidence interval, 1.0–8.4) and a dose in target range (odds ratio, 5.5; 95% confidence interval, 1.5–20.4) were significantly associated with the risk of having movement disorders.

Conclusions: The prevalence of movement disorders in people with ID and behavioral problems is high, especially in ID patients using antipsychotics. More attention is needed for these movement disorders and their potential impact.

Key Words: antipsychotics, movement disorders, intellectual disability

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The prevalence of behavioral problems in people with intellectual disability (ID) varies from 20% to over 50%, depending on the setting and the definition of behavioral problems.[1–4] Treatment of these behavioral problems with psychotropic medication, especially antipsychotics, is common even though there is a lack of evidence of effectiveness.[5–9] Approximately 30% to 40% of intellectually disabled adults use antipsychotic drugs, often for many years and sometimes even decades.[1,2,10,11] The long-term use of antipsychotic drugs increases the potential of harmful adverse effects, including movement disorders. Movement disorders associated with antipsychotic drug use consist of akathisia, dystonia, dyskinesia, and parkinsonism[12] and can have a major negative impact on the quality of life of patients. They may interfere with activities of daily living and integration into society.[13,14] There are few studies that assessed the prevalence of movement disorders in people with ID in general.[11,15] These earlier studies, however, lacked standardized assessments or focused only on dyskinesia. They did find an association with psychotropic drug use, especially antipsychotic drugs. The aim of the present study was to examine the prevalence of the 4 main movement disorders (dyskinesia, akathisia, dystonia, and parkinsonism) using a standardized and validated (in psychiatric patients) assessment in in-patient adults with mild ID and behavioral problems and to evaluate the association with use of antipsychotics.

METHODS

Setting

The participants for the current study were recruited from 3 Dutch institutions specialized in treating patients with mild to borderline ID and behavioral problems. Adults with ID are referred to these institutions if treatment in general mental health institutions and/or specialized units of residential settings did not lead to satisfactory results regarding behavioral problems. The medical ethics committee of the University Medical Centre Utrecht approved the study.

Participants

All patients admitted to these centers were eligible if they were mentally capable of making the decision of participating in this study. In the participating facilities, all eligible patients were informed about the study and its goals and gave permission through an informed consent procedure. We included patients in the period from August 2009 to October 2011. These patients had mild/borderline ID with a level of intellectual functioning between 50 and 90. Both patients admitted to the centers before the start of the study period, and patients newly admitted during the study period were included.

Assessment of Movement Disorders

The main outcome measure was the prevalence of the 4 movement disorders (dyskinesia, akathisia, parkinsonism, and dystonia). They were measured by 1 trained physiotherapist using a standardized protocol.[16,17]

Dyskinesia was assessed with the Abnormal Involuntary Movement Scale,[18] and case definition was based on Schooler and Kane criteria.[19] Presence of dyskinesia was scored if there was at least moderate dyskinesia in 1 body area or at least mild dyskinesia in 2 body parts. The Barnes Akathisia Rating Scale[20] was used for assessing akathisia, comprising both objective and subjective items. A score of at least mild was required. Parkinsonism was assessed with the motor examination part of the Unified Parkinson Disease Rating Scale.[21] This was scored if there was

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at least mild expression of rest-tremor or rigidity or 1 rating of at least moderate expression of bradykinesia and postural instability or 2 ratings of at least mild bradykinesia and postural instability. For bradykinesia and postural instability, a higher cutoff point was used because these symptoms may also be part of psychiatric syndromes or sedation. Dystonia was assessed with 1 separate item. Therefore, a score of at least mild was required.[16]

Association With Antipsychotic Drug Use

To determine the association between antipsychotic drug use and movement disorders, the prevalence of antipsychotic drug use was compared between participants with and without movement disorders. Information on medication use was collected through the institutions' pharmacy information systems and available from the date of admission of the patient onwards. Medication was coded according to the World Health Organization Anatomic Therapeutic Chemical classification system.[22]

Antipsychotic drug use in the 3 months before the index date was examined. The index date was the day of assessment of movement disorders. If the date of admission to the institution was within these 3 months, the antipsychotic drug use during this shorter duration of stay was examined. Use of any antipsychotic drug, number of different antipsychotics (1 or ≥2 antipsychotic drugs), and use typical or atypical antipsychotics in the 3 months before index date was studied. The use of the different types of antipsychotic drugs on index date was assessed. The dose of antipsychotic drugs on index date was categorized in low dose, dose in target range, and maximum dose according to the International Consensus Study of Antipsychotic Dosing by Gardner et al.[23] Of the 2 antipsychotic drugs (pipamperone and penfluridol) not mentioned in the study of Gardner et al, the low dose and dose in target range were defined as follows: the cutoff value used for pipamperone was 40 mg/d, and for penfluridol, it was 20 mg/wk.

Potential Confounders

For the baseline characteristics, data were collected from the standardized basic registration lists that are in use in all 3 participating centers. These lists were filled in by the therapists of the patients and contained demographic information (eg, age, sex, ethnic background) and information on hospitalization in the center (eg, duration of stay at the day of measurement and codes of *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* [*DSM-IV*] disorders or descriptive diagnoses).

Diagnoses were coded by the physician according to *DSM-IV* (American Psychiatric Association, 2000), and if these were not available, the descriptive diagnosis was used. Diagnoses were categorized into the following main diagnostic categories: psychotic disorders, pervasive developmental disorders, attention-deficit/hyperactivity disorder (ADHD) and conduct disorders, mood disorders, anxiety disorders, alcohol/drug dependence or abuse, personality disorders, sexual disorders, and other diagnoses. The categorization was performed by authors S.W. and A.S.

Level of intellectual functioning was available from the patient records and assessed by means of standard intelligence tests (eg, WAIS-III, GIT-2, WISC-R). If IQ was not available, the *DSM-IV* diagnosis was used. The level of intellectual functioning was categorized in the following: moderate ID (IQ range, 35–50), mild ID (IQ range, 51–70), borderline intellectual functioning (IQ range, 71–84), below average intelligence (IQ range, ≥85–90), and unspecified.

The following medication groups were distinguished as drugs for a psychiatric indication (psychotropic drugs): antipsychotics, antidepressants, mood stabilizers, psychostimulants (agents used for ADHD), benzodiazepines, drugs used in addictive disorders, and anticholinergics. All nonpsychotropic drugs were categorized as somatic medications. Anticonvulsants used specifically for epilepsy were categorized under the somatic medication label instead of as a mood stabilizer. Use of any medication, any somatic medication, and any psychotropic drug in 3 months before index date were assessed.

Data Analysis

The baseline characteristics, the medication databases, and information on movement disorders were linked anonymously through record linkage methodology based on an identification number. Data were analyzed using IBM SPSS Statistics for Windows, Version 20 (IBM Corp, Armonk, NY). The overall prevalence of movement disorders was assessed, with the total number of patients with movement disorders divided by the total number of included patients. In addition, prevalence of the several distinct movement disorders (dyskinesia, akathisia, dystonia, and parkinsonism) was assessed. The association of antipsychotic drugs in relation to movement disorders was studied. Odds ratios (OR) were calculated using logistic regression analysis. All potential confounders were tested in this logistic regression model; if they changed the unadjusted OR by more than 10%, they were included in the final model.

RESULTS

Population

Of the complete population in the participating institutions, approximately 10% of patients were not mentally capable to provide informed consent. One third of the remaining patients participated, resulting in a total of 134 patients with ID and severe behavioral problems that were included in the study. Approximately three quarters were male and a quarter was female (Table 1). The mean age was 31.4 years, ranging from 15 to 64 years. Many patients had a diagnosis of alcohol/drug dependence or abuse (52 patients), a personality disorder (43 patients), a psychotic disorder (36 patients), and ADHD/conduct disorder (32 patients). The majority of patients had mild ID or borderline intellectual functioning. The mean duration of stay was 21.9 months, ranging from 1 week to 227 months.

Prevalence of Movement Disorders

Of 134 adults in total, 59 (44.0%) had at least 1 movement disorder (Table 1). Forty-one percent of the male and 52.9% of the female patients had any movement disorder. Patients older than the age of 30 years had more movement disorders than the age group younger than 30 years (50% vs 39.7%). It turned out that the majority of the patients with a *DSM-IV* diagnosis had at least 1 movement disorder; 69.4% of the adults with a psychotic disorder, 58.3% with an anxiety disorder, 55.6% with a mood disorder, and 51.2% with a personality disorder.

In Figure 1, a Venn diagram of the prevalence of movement disorders is shown, including the percentages of the overlapping movement disorders. Parkinsonism occurred in 36.6%, dyskinesia in 11.2%, akathisia in 9.0%, and dystonia in 0.7%.

Prevalence of Antipsychotic Drug Use and Associations With Movement Disorders

Table 2 shows the prevalence of antipsychotic drug use in the 3 months before index date. More than three quarters of patients with movement disorders used any antipsychotic drug, while this was the case for about half of patients without any movement disorder. A substantial amount used 2 or more antipsychotic drugs.

TABLE 1. Baseline Characteristics and Prevalence of Medication Use and Movement Disorders (N = 134)

Baseline Characteristics	Patient, n	Patient With Movement Disorders, n (%)
Total	134	59 (44.0)
Sex		
Male	100	41 (41.0)
Female	34	18 (52.9)
Age, y		
≤30	78	31 (39.7)
>30	56	28 (50.0)
Ethnic background*		
Dutch parents	98	46 (46.9)
Other	19	7 (36.8)
DSM-IV diagnosis†		
Psychotic disorder	36	25 (69.4)
Mood disorder	9	5 (55.6)
Anxiety disorder	12	7 (58.3)
Alcohol/drug dependence or abuse	52	23 (44.2)
ADHD and conduct disorder	32	10 (31.3)
Pervasive developmental disorder	27	11 (40.7)
Sexual disorder	10	5 (50.0)
Personality disorder	43	22 (51.2)
ID (IQ)*		
≤50	2	2 (100.0)
51–70	58	26 (44.8)
71–84	58	24 (41.4)
≥85–90	6	4 (66.7)
Admission time, mo*		
0–6	46	16 (34.8)
6–12	26	13 (50.0)
>12	61	30 (49.2)
Use of any medication in 3 mo before index date‡	122	54 (42.9)
Use of any somatic medication in 3 mo before index date‡	104	48 (46.2)
Use of any psychotropic drug in 3 mo before index date‡	105	53 (50.5)

*Totals do not add up to 100% due to missing data.

†Patients can have more than 1 *DSM-IV* diagnosis.

‡Missing data for 8 patients.

Patients with movement disorders used more typical antipsychotics than atypical antipsychotics (50.8% vs 44.1%) in contrast to patients without movement disorders (25.3% vs 34.7%). Of the antipsychotic drugs, the specific types on index date were assessed as well. Risperidone (n = 16), haloperidol (n = 14), zuclopenthixol (n = 13), pipamperone (n = 11), and olanzapine (n = 11) were the most commonly prescribed. Furthermore, these antipsychotics were more often prescribed in adults with movement disorders, and a large majority used a dose in the target range on index date.

Odds ratios were calculated and adjusted for these confounding factors: sex, age, ethnic background, duration of stay, IQ, ADHD/conduct disorders, mood disorders, anxiety disorders, psychotic disorders, pervasive developmental disorders, alcohol/drug dependence or abuse, sexual disorders, and personality disorders. The use of any antipsychotic drug (OR, 3.0; 95% confidence interval [CI], 1.0–8.4), use of typical antipsychotics (OR, 2.9; 95% CI, 1.2–7.1), use of a dose of antipsychotics in target range (OR, 5.5; 95% CI, 1.5–20.4), and use of a maximum dose (OR, 5.4; 95% CI, 1.0–29.0) statistically and significantly increased the risk of having movement disorders. Using 2 or more antipsychotic drugs increased the risk of having movement disorders (OR, 6.3; 95% CI, 1.5–26.1) compared with use of 1 antipsychotic drug (OR, 3.6; 95% CI, 1.1–12.2).

DISCUSSION

The present study showed that almost half (44.0%) of 134 in-patient adults with mild ID and behavioral problems had at least 1 movement disorder. Parkinsonism occurred in 36.6%, dyskinesia in 11.2%, akathisia in 9.0%, and dystonia in 0.7%. There is a significant increased risk on movement disorders with the use of antipsychotic drugs, especially using more antipsychotic drugs, typical antipsychotic drugs, and a higher dose.

In a previous study on the presence of movement disorders in 99 adults with ID on long-term antipsychotic medication conducted by de Kuijper et al, an even higher prevalence of movement disorders (53%) was found: 38% had dyskinesia, 20% had parkinsonism, and 22% had akathisia.[11] Matson et al[15] found a prevalence of 45.1% of tardive dyskinesia in 264 adults with mild to profound ID and long-term psychotropic use, using the Matson evaluation of drug adverse effects and the Dyskinesia Identification System Condensed User Scale. Dyskinesia occurs mostly after a long period of antipsychotic drug use as seen in both studies of de Kuijper et al and Matson et al. In the current study, the total duration of antipsychotic drug use is unknown; a possible shorter period of use might explain the lower prevalence of dyskinesia. De Kuijper et al only measured the dyskinesia with a standardized measurement scale, the Abnormal Involuntary Movement Scale; parkinsonism and akathisia were assessed by physical examination. This might explain the difference in the prevalence of parkinsonism and akathisia. Other explanations could be difference in study population (severity of ID) or difference in antipsychotic drug dose.

Matson et al[15] found a similar association of dyskinesia with antipsychotic drug use and with total psychotropic daily dose; however, they did not mention the antipsychotic dose specifically. De Kuijper et al[11] found a higher dose of antipsychotic drugs to be associated with a greater severity of parkinsonism. In the current study, the focus was on the 4 movement disorders together and the association with antipsychotic drug use and dose in detail. As far as we know, apart from the studies mentioned previously, this is the first study in people with ID to measure the movement disorders in this systematic way and to examine the association with antipsychotic drugs in this detail.

Our population is similar to a psychiatric population when compared with a study in psychiatric patients without ID. The prevalence of movement disorders in 194 long-stay psychiatric patients without ID was 56.2% for parkinsonism, 28.4% for tardive dyskinesia, 5.7% for tardive dystonia, and 4.6% for akathisia.[12] However, our study included mainly people with mild ID to borderline intellectual functioning, only 2 with moderate ID, and no people with severe ID. It has also been found that these movement disorders occur in psychiatric patients without using antipsychotic drugs, so this suggests that these symptoms may also be related to the illness itself rather than just the result of antipsychotic drugs.[24,25] This can also be the case with ID, especially when this is caused by brain damage.[26] The population of the present study consisted only of adults with ID, so the influence of intellectual disabilities could not be studied. For future research, it is

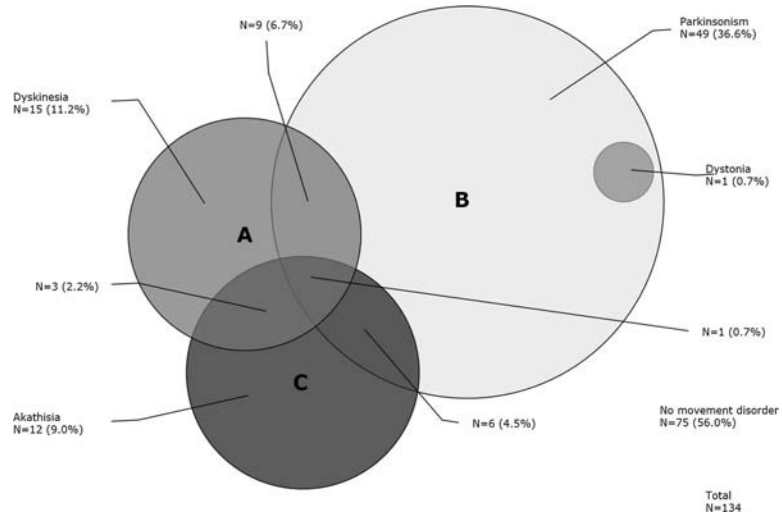

FIGURE 1. Venn diagram of the prevalence and overlap of movement disorders (n = 134). The different movement disorders occurred both alone and in combination with other movement disorders. Only dyskinesia occurred in n = 4 and in combination with other movement disorders in n = 11, only parkinsonism in n = 34 and in combination in n = 15, only akathisia in n = 4 and in combination in n = 8, and only dystonia in n = 0 and in combination in n = 1.

TABLE 2. Prevalence of Antipsychotic Drug Use in Patients With and Without Movement Disorders (N = 134)

	Patient With Movement Disorders (n = 59), n (%)	Patient Without Movement Disorders (n = 75), n (%)	OR (95% CI)	Adjusted OR (95% CI)*
Use of any antipsychotic drug in 3 mo before index date	46 (78.0)	39 (52.0)	**3.3 (1.5–7.0)**	**3.0 (1.0–8.4)**
1 antipsychotic drug	28 (47.5)	27 (36.0)	**4.3 (1.7–10.9)**	**3.6 (1.1–12.2)**
≥2 antipsychotic drugs	18 (30.5)	12 (16.0)	**6.2 (2.1–17.9)**	**6.3 (1.5–26.1)**
Typical antipsychotics in 3 mo before index date[†]	30 (50.8)	19 (25.3)	**3.0 (1.5–6.3)**	**2.9 (1.2–7.1)**
Atypical antipsychotics in 3 mo before index date[†]	26 (44.1)	26 (34.7)	1.5 (0.7–3.0)	1.1 (0.5–2.8)
Type of antipsychotic on index date[‡]				
Zuclopenthixol	10 (16.9)	3 (4.0)	**5.2 (1.4–20.1)**	**9.2 (1.3–63.8)**
Haloperidol	9 (15.3)	5 (6.7)	2.7 (0.8–8.5)	2.5 (0.6–10.4)
Pipamperone	7 (11.9)	4 (5.3)	2.5 (0.7–9.1)	4.0 (0.8–21.1)
Risperidone	7 (11.9)	9 (12.0)	1.0 (0.4–3.0)	0.6 (0.2–2.2)
Olanzapine	7 (11.9)	4 (5.3)	2.5 (0.7–9.1)	6.7 (0.9–49.1)
Clozapine	5 (8.5)	4 (5.3)	1.7 (0.4–6.8)	0.7 (0.1–3.9)
Aripiprazole	5 (8.5)	2 (2.7)	3.6 (0.7–19.2)	3.0 (0.4–21.6)
Quetiapine	1 (1.7)	4 (5.3)	0.3 (0.0–3.0)	0.3 (0.0–5.0)
Other[§]	6 (10.2)	7 (9.3)	1.2 (0.4–3.7)	0.8 (0.2–3.4)
Dose of antipsychotic on index date[‖¶]				
No antipsychotic use	10 (16.9)	37 (49.3)	Reference	Reference
Low dose	8 (13.6)	10 (13.3)	3.0 (0.9–9.5)	3.1 (0.6–15.2)
Dose in target range	27 (45.8)	20 (26.7)	**5.0 (2.0–12.4)**	**5.5 (1.5–20.4)**
Maximum dose	9 (15.3)	5 (6.7)	**6.7 (1.8–24.4)**	**5.4 (1.0–29.0)**

Significant associations are printed in bold ($P < 0.05$).

*Adjusted for sex, age, ethnicity, duration of stay, IQ, ADHD/conduct disorders, mood disorders, anxiety disorders, psychotic disorders, pervasive developmental disorders, alcohol/drug dependence or abuse, sexual disorders, and personality disorders.

[†]Sixteen patients used typical and atypical antipsychotics simultaneously.

[‡]Number of antipsychotic drug differs between period of 3 mo before index date and on index date.

[§]Other antipsychotic drugs: chlorprothixene (5), pimozide (3), penfluridol (1), levomepromazine (2), fluspirilene (1), periciazine (1).

[‖]Totals do not add up to 100% due to missing data.

[¶]Grouping according to Gardner et al (1), except for pipamperone and penfluridol for which the cutoff value used for pipamperone was 40 mg/d and for penfluridol 20 mg/wk.

recommended to study the influence of presence of an ID with regard to the presence of movement disorders.

In the discussion about the prevalence of movement disorders caused by the so-called typical (or first generation) or atypical (second generation) antipsychotic drugs, at first typical antipsychotic drugs were associated with more movement disorders. In some recent studies, however, it turned out that the prevalence of movement disorders is probably equivalent with typical and atypical antipsychotics.[27,28] In our study, this could not be confirmed. Use of typical antipsychotics in the period of 3 months before index date was significantly associated with the presence of movement disorders in contrast to use of atypical antipsychotics.

Strengths and Limitations

This is one of the first studies, which measured the prevalence of several movement disorders (dyskinesia, akathisia, dystonia, and parkinsonism) with a standardized and validated assessment in this specific population. However, some of these assessments are only validated in psychiatric patients without ID. The assumption is that these patients were mentally capable in making the decision to participate and performing the simple exercises that were used for assessing the movement disorders. So the difference with the psychiatric population should be minimal. As the movement disorders in the current study were measured by a single, specifically trained physiotherapist, all patients were examined in the same way.

Another strength of this study is that accurate and complete pharmacy data were available and that demographic data and information about hospitalization in the centers could be extracted from basic registration lists, which also included *DSM-IV* diagnoses and level of intellectual functioning.

A limitation is that the type and dose of antipsychotic medication could have been changed in the period before admission to the institutions. It was not possible to investigate this medication. Because tardive disorders are often irreversible, it could be that patients have discontinued antipsychotic medication long before the study period and still present movement disorders. This would result in an underestimation of the risk. On the other hand, some antipsychotics may have been prescribed to prevent movement disorders, such as clozapine in patients with dyskinesia, which could lead to an overestimation of the risk. To fully understand the relationship between antipsychotic medication use and movement disorders, patterns of use over time should be studied.

Not all patients had a diagnosis in accordance with the *DSM-IV*, sometimes only a descriptive diagnosis was available. The medication data were collected from pharmacy databases; however, there was no information about the reasons for prescription of the medications. The level of intellectual functioning should be present in the basic registration lists of the centers, but still not always traceable in clinical records, and in some instances, the determination of level of intellectual functioning was conducted quite some time in the past. All patients were supposed to have an ID, but this was not always shown from the data (ie, 6 of the 134 participants had an IQ between 85 and 90). Patients with more severe intellectual disabilities and/or behavioral problems are likely to not have participated, resulting in a selection of participants in this study.

CONCLUSIONS

The high prevalence of movement disorders is worrisome because it can be very debilitating for these patients. It is important to create awareness of this high prevalence among the patients themselves and the physicians. Many patients are unaware of movement disorders. Physicians might think that symptoms belong to the underlying disorder, for example, the ID or a psychotic disorder. Another important aspect is that many adults with ID and behavioral problems use antipsychotic drugs for many years, sometimes even decades, without discontinuing this medication. Adverse effects are therefore present for a very long time, which might explain why many physicians fail to recognize adverse effects. Akathisia may even be misdiagnosed as a behavioral problem. Standardized systematic investigation of drug-induced movement disorders can improve recognition. It is important to continuously weigh the benefits and risks of antipsychotic medication use. Discontinuation or dose lowering of antipsychotic drugs should be considered when movement disorders are invalidating the quality of life of a patient. When discontinuation of medication is considered, this should involve the multidisciplinary team and the environment of the adults with ID in order for it to be successful.[29,30] Future research is necessary to create more awareness among physicians and to teach them how to reduce or even prevent these movement disorders.

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AUTHOR DISCLOSURE INFORMATION

The authors declare no conflicts of interest.

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