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Screening for depression in youth with epilepsy: Psychometric analysis of NDDI-E-Y and NDDI-E in a French population

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ABSTRACT

Objectives: The objective of this study was to evaluate the Neurological Disorders Depression Inventory-Epilepsy (NDDI-E) for Youth (NDDI-E-Y) for screening for major depressive disorder (MDD) in French youth with epilepsy (YWE), in order to (1) validate this tool in a separate population; (2) determine whether the 12-item NDDI-E-Y affords advantages over the 6-item adult NDDI-E; (3) measure psychometric performance of each item.
Methods: Youth with epilepsy aged 11–17 years completed a 15-item questionnaire to calculate total scores for NDDI-E-Y (12 items) and NDDI-E (6 items). Gold standard for MDD was Children's Depression Inventory (CDI). Receiver operator characteristic (ROC) analyses for total NDDI-E-Y and NDDI-E scores were compared. Psychometric properties of each item were analyzed for: floor/ceiling effect, item-internal consistency, and ROC curve.
Results: Ninety-seven YWE were included; 21.6% had MDD (CDI > 15). Correlation was very high between total NDDI-E-Y and NDDI-E scores, and high between NDDI-E-Y and CDI. Cutoff point for the NDDI-E-Y maximizing both sensitivity and specificity was 23 (original study cutoff 32). The ROC analysis of the NDDI-E-Y showed an area under the curve (AUC) 0.967 (95% confidence intervals [CI] 0.909–0.992); ($p < 0.0001$). Sensitivity, specificity, and positive (PPV) and negative predictive values (NPV) were 100% [83.9; 100], 82.9% [72.5; 90.6], 61.8 [43.6; 77.8], and 100% [94.3; 100], respectively. The NDDI-E-Y was not superior to NDDI-E according to pairwise comparison of ROC ($p = 0.07$). Psychometric analysis revealed marked differences between items. After eliminating items with poorer performance, a 6-item version of the NDDI-E-Y showed sensitivity, specificity, PPV, and NPV of 100% [85.5; 100], 85.5% [75.6; 92.5], 65.6 [46.8; 81.4], and 100% [94.5; 100], respectively. This was significantly better than the adult NDDI-E ($p = 0.03$) though not NDDI-E-Y ($p = 0.07$).
Significance: Significant difference in cutoff indicates that the NDDI-E-Y cannot yet be recommended for widespread screening of MDD in YWE. Discrepancies in psychometric performance between items suggest that further work is needed to examine both validation of the original 12-item NDDI-E-Y and comparison with a shorter version.

1. Introduction

Major depressive disorder (MDD) or depressive symptoms are present in 10–30% youth with epilepsy (YWE) [1–4], who are at higher risk of presenting MDD than healthy peers or youth with other chronic health problems [5], producing significantly negative effects on quality of life (QoL) [6]. Suicidal ideation is also common in YWE [7]. However, MDD in YWE remains underdiagnosed and undertreated [8], in part because of symptomatic overlap with side effects of antiepileptic drugs (AEDs) and atypical depressive symptoms in adolescence such as irritability, attention deficit, fatigue, and sleep complaints [9]. The International League Against Epilepsy (ILAE) emphasizes the importance of screening for MDD in routine practice when evaluating patients with epilepsy [8], and development of specific screening tools adapted for the pediatric population with epilepsy have been identified as a pressing need [6,10]. However, developing screening instruments in YWE is a more complex process than for adults, because of the need to choose

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items that are readily understood by younger subjects, and difficulty for the younger patient in evaluating emotions based on a quantified score [11]. This diagnostic challenge led to the development of the Neurological Disorders Depression Inventory-Epilepsy (NDDI-E) for Youth (NDDI-E-Y) proposed by Wagner and colleagues [9,12]. They first developed an 11-item version of the NDDI-E-Y [9], based upon the previously well-validated 6-item NDDI-E for adults [13]. A subsequent 12-item version of the NDDI-E-Y was then proposed by the same authors, validated in a 2-center United States outpatient population of 12- to 17-year-old YWE [12]. Compared to the 6-item adult NDDI-E, the NDDI-E-Y includes extra items pertaining to symptoms of loneliness and irritability, relevant to particular aspects of MDD in this age group, and in addition certain items of the NDDI-E were removed according to expert opinion [12]. Psychometric properties of the NDDI-E-Y have been demonstrated to be satisfactory in this single study [12], but to date no other study has confirmed the psychometric properties of the NDDI-E-Y. This is in contrast to the NDDI-E for screening for MDD in adults, which has been validated in over 10 languages [14], showing very stable properties across global populations [10,15]. In addition, while the goal of the NDDI-E-Y was to provide a tool that is better adapted to specific challenges of screening for MDD in YWE, demonstration of specific advantages of the 12-item NDDI-E-Y over the original 6-item NDDI-E in this age group has not been provided, and no previous study has directly compared these in an adolescent population.

The aim of the present study was twofold: (1) to measure psychometric performance of the NDDI-E-Y in a separate population; (2) to determine whether the 12-item NDDI-E-Y affords specific advantages over the 6-item NDDI-E in screening for MDD in YWE, and to perform psychometric analysis of each item in both questionnaires. To this end, we conducted a validation study of a French translation of the NDDI-E-Y and prospectively compared NDDI-E and NDDI-E-Y in the same population.

2. Material and methods

2.1. Translation of the NDDI-E-Y

Forward–backward translation was performed, following standard practice for screening tool multilanguage validation studies [16], and as performed by our group in a previous study for the NDDI-E [14]. The original United States English version was translated into French independently by two native French speakers, a psychiatrist (JAMF) and a child psychiatrist (MV). Back-translation into English was undertaken by a neurologist and native English speaker (AMG), independently of the forward-translation. Concerning items for which cross-language agreement could not be reached, French sentences were reworked until all authors agreed. The final questionnaire was tested for comprehension and cultural acceptability in a random sample of 5 YWE during routine outpatient consultation, and no changes to the text were considered necessary. See Table 1 for items of the NDDI-E-Y (items 1–12 in the table).

2.2. Participants

Subjects were recruited from March 2017–June 2018 from 2 epilepsy centers in Marseille, France. Inclusion criteria were as follows: native French-speaking adolescents aged 11–17 years with any type of epilepsy according to the ILAE criteria, with onset of epilepsy at least 1 year before, without significant cognitive impairment. Cognitive abilities were confirmed with neuropsychological assessment where possible; otherwise, ability to participate in an ordinary class was taken into account. Diagnosis of epilepsy was documented clinically, confirmed where necessary with video-electroencephalography (EEG). Inpatients and outpatients were included. Exclusion criteria included inability to understand and answer the self-report questionnaires and severe mental illness. Gender, age, type and frequency of seizures, age at onset of epilepsy, number of antiepileptic drugs (AEDs), other medication, and educational level were collected.

2.3. Measures

Subjects completed the 12-item NDDI-E-Y in order to evaluate depressive symptoms over the preceding 2-week period. We wished to follow the same methodology as that used by the team that developed the NDDI-E-Y. Therefore, each item was initially rated by the adolescent as "never" (score = 0), "rarely" (score = 1), "sometimes" (score = 2), or "always or often" (score = 3) according to the methodology reported by Wagner and colleagues [12,17]. However, in the course of our study, preliminary results showed very marked discordance with those reported by Wagner and colleagues in terms of cutoff, leading us to verify with the authors the methodology of the original study. Subsequently, published correspondence [12,13] confirmed an error in their reported Likert scoring scale, which should have been 1–4 rather than 0–3 (erratum published [18]). Thus, the correct scoring system, which was used to calculate NDDI-E-Y scores, ranged from "never" (score = 1), "rarely" (score = 2), sometimes (score = 3), to "always or often" (score = 4), corresponding to a maximum of 48. The correct scoring system for the NDDI-E-Y is thus similar to that of the adult NDDI-E.

Of the 12 items in the NDDI-E-Y (Table 1), 3 also belong to the adult NDDI-E: item 1 "Everything is a struggle"; item 4 "I feel frustrated"; and item 10 "I feel guilty". In order to test all items of both the 12-item NDDI-E-Y and the 6-item adult NDDI-E, we added the 3 remaining items of the NDDI-E at the end of the questionnaire ("Nothing I do is right"; "Difficulty finding pleasure"; and "I'd be better off dead"), making a total of 15 items from which both the 12-item NDDI-E-Y and 6-item NDDI-E total scores could be calculated. These 15 items are shown in Table 1 (Items 1–12 = NDDI-E-Y; items 13–15 = remaining 3 items of the NDDI-E that do not appear in the NDDI-E-Y).

All subjects also completed the Children's Depression Inventory (CDI) [14,15], a 27-item multiple-choice questionnaire assessing the severity of depressive symptoms during the previous 2 weeks. For each item, children choose between 3 responses corresponding to a rating of 0, 1, or 2 according to symptom severity. Total scores range from 0 to 54, higher scores representing more severe depression. The CDI scores > 15 are considered a clinically meaningful cutoff score to identify MDD for French youth [19,20]. The CDI was used as gold standard for the diagnosis of current MDD in YWE; we wished to reproduce as closely as possible the methodology of the original NDDI-E-Y validation, but the CDI-2 as used by Wagner and colleagues is not available in a French version, and the CDI was therefore selected as the most appropriate alternative.

The NDDI-E-Y and CDI were completed by subjects in the presence of the doctor (NV, MM, AL, AMG), who could be asked for clarification of the meaning of any item.

Additional clinical evaluation of depressive symptoms was also carried out by the doctor using the Children's Depression Rating Scale–Revised (CDRS-R) [21,22], the most widely used rating scale for assessing severity of depression and change in depressive symptoms for clinical research trials in children and adolescents with depression [23]. The CDRS-R is a 17-item scale, with items ranging from 1 to 5 or 1 to 7 (possible total score from 17 to 113), rated by a clinician via interviews with the child and parent. A score of 40 is indicative of MDD, whereas a score of 28 is often used to define remission (minimal or no symptoms). Prior to using this scale, child neurologists received brief training and explanation of use of the CDRS-R by the child psychiatrist (MV).

2.4. Procedure

Adolescents and their caregivers were invited to participate during routine epilepsy outpatient visit or hospital stay for video-EEG; all

Table 1
English version/French version and mean standard deviation and frequency of response for each of item of the NDDI-E-Y and NDDI-E. Based on results of psychometric testing of each item, items highlighted in gray were retained as the most pertinent and were tested as a short 6-item version of the NDDI-E-Y (see Results and Supplementary material).

	Scale	Items	Mean	SD	ROC area	Never / Jamais 1	Rarely / Rarement 2	Sometimes / Parfois 3	Alwas or often / Toujours ou souvent 4
1	NDDI-E NDDI-E-Y	Everything is a struggle / Tout est une lutte	2.13	1.06	0.829	38.1	22.7	26.8	12.4
2	NDDI-E-Y	I have trouble finding anything that makes me happy / J'ai du mal à trouver quoi que ce soit qui me rend heureux	1.53	0.77	0.745	62.9	21.6	14.4	1
3	NDDI-E-Y	I feel like crying / J'ai envie de pleurer	1.89	0.94	0.785	43.3	29.9	20.6	6.2
4	NDDI-E NDDI-E-Y	I feel frustrated / Je me sens frustré(e)	2.00	0.97	0.804	38.1	33	19.6	9.3
5	NDDI-E-Y	I feel unhappy / Je me sens malheureux (se)	1.65	0.87	0.889	56.7	24.7	14.4	4.1
6	NDDI-E-Y	I think about dying or killing myself / Je pense à mourir ou à me tuer	1.23	0.59	0.791	83.5	10.3	5.2	1
7	NDDI-E-Y	Nothing I do is ever right / Je ne fais jamais rien de bien	1.75	0.92	0.712	51.5	27.8	14.4	6.2
8	NDDI-E-Y	I feel sorry about things / Je me sens désolé(e) pour des choses	2.17	0.97	0.752	28.9	36.1	23.7	11.3

9	NDDI-E-Y	I feel sad / Je me sens triste	2.02	1.0A	0.868	39.2	29.9	20.6	10.3
10	NDDI-E NDDI-E-Y	I feel guilty / Je me sens coupable	1.70	.94	0.805	55.7	26.8	9.3	8.2
11	NDDI-E-Y	I feel cranky or irritated / Je me sens grincheux (se) ou irrité(e)	2.17	1.05	0.828	35.1	24.7	27.8	12.4
12	NDDI-E-Y	I feel alone / Je me sens seule	1.72	0.98	0.787	56.7	23.7	10.3	9.3
13	NDDI-E	Nothing I do is right / Rien de ce que je fais n'est bien	1.64	0.81	0.779	54.6	27.8	15.5	2.1
14	NDDI-E	I'd be better off dead /Je ferai mieux d'être mort(e)	1.15	0.52	0.679	89.7	7.2	1	2.1
15	NDDI-E	J'ai des difficultés à trouver du plaisir	1.50	0.86	0.776	69.1	16.5	9.3	5.2

gave informed consent. The YWE completed the 15-item questionnaire containing the 12-items of the NDDI-E-Y plus the 3 additional items from the adult NDDI-E as described above, and the CDI. The CDRS assessments were also carried out in the same visit, and demographic and clinical details noted.

Adolescents and families received no compensation for their participation, in accordance with French regulations and in contrast to the study by Wagner et al. [12]. This study was conducted in accordance with the Declaration of Helsinki and the Ethics Committee of Aix-Marseille University.

2.5. Statistical analyses

Descriptive statistics of the obtained data included frequencies and percentages of categorical variables together with means and standard deviations of continuous variables. Demographical and clinical data were compared between YWE with and without MDD using Chi^2 test for categorical variables and Student's *t*-test for continuous variables.

For the validation process, we analyzed psychometric properties of the French NDDI-E-Y version including internal structural validity, external validity, and receiver operator characteristics. Data analysis was performed using SPSS software (Version 18 for Mac, PASW Statistics) and MedCalc software (Version 14.8 for Windows). For all tests, significance level was 5%.

2.6. Internal structural validity

Floor and ceiling effects were used to assess response distribution for the 12 items in the NDDI-E-Y and the 3 remaining items of the NDDI-E. The rate of floor and ceiling effects were calculated as the proportion of individuals who obtained the lowest ("never") and the highest ("always or often") scores for any of the items. Correlations between each of the 15 items were performed using Pearson's coefficient.

For the 12 items of the NDDI-E-Y, item-internal consistency was assessed by correlating each item with the overall corrected scores using Pearson's coefficient; correlations of at least 0.4 are recommended for supporting item-internal consistency. Internal consistency reliability was assessed by Cronbach's alpha coefficient. It was recalculated after items were removed. To confirm consistency, a coefficient of at least 0.7 was expected for each item removed.

2.7. External validity

To explore external validity, relations between the 12-item NDDI-E-Y and the 6-item NDDI-E, the CDI and the CDRS-R were investigated by computing Pearson's coefficients.

2.8. Receiver operator characteristics

Receiver operator characteristics (ROC) were analyzed to assess the utility of the NDDI-E-Y overall score in detecting MDD defined by the

Table 2
Demographic and clinical characteristics.

	Total	YWE without MDD	YWE with MDD	
	n = 97	n = 76	n = 21	p-Value
Age in years (M ± SD)	14.9 ± 1.7	14.9 ± 1.7	15 ± 1.5	0.8075
Gender (female)	52 (53.6%)	39 (51.3%)	13 (61.9%)	0.3911
Age at onset in years (M ± SD)	8.4 ± 3.9	8.1 ± 4.0	9.5 ± 3.5	0.1487
Time since epilepsy diagnosis in years	6.5 ± 4.0	6.8 ± 4.2	5.5 ± 3.2	0.1917
Antiepileptic drugs				
Monotherapy	67 (69.1%)	55 (72.4%)	12 (57.2%)	0.1843
Dual therapy	23 (23.7%)	19 (25%)	4 (19%)	0.5691
Polytherapy	7 (7.2%)	2 (2.6%)	5 (23.8%)	**0.0009**
Seizure type				
Generalized	50 (51.5%)	41 (53.9%)	9 (42.8%)	0.3701
Partial	47 (48.5%)	35 (46.1%)	12 (57.1%)	
Lobe				
Temporal	17 (36.2%)	14 (40%)	3 (25%)	0.3559
Extratemporal	30 (63.8%)	21 (60%)	9 (75%)	
Frequency of seizures				
0	41 (42.3%)	36 (47.4%)	5 (23.8%)	0.0539
<1 per month	33 (34%)	25 (32.9%)	8 (38.1%)	0.6578
1–3 per month	12 (12.4%)	7 (9.2%)	5 (23.8%)	0.0734
≥1 per week	11 (11.3%)	8 (10.5%)	3 (14.3%)	0.6284
CDI total score (M ± SD)	10.4 ± 7.1	7.3 ± 3.3	21.5 ± 6.0	<**0.0001**
CDRS-R	31.2 ± 13.9	26.7 ± 7.7	47.8 ± 18.3	<**0.0001**
NDDI-E-Y (M ± SD)	22.0 ± 7.4	19.1 ± 5.0	32.4 ± 4.9	<**0.0001**
NDDI-E (M ± SD)	10.14 ± 3.7	8.4 ± 2.7	14.8 ± 2.9	<**0.0001**

M, mean; SD, standard deviation; CDI, Children's Depression Inventory; CDRS-R Children's depression rating scale-revised (CDRS-R); NDDI-E-Y, Neurological Disorders Depression Inventory in Epilepsy-Youth; NDDI-E, Neurological Disorders Depression Inventory in Epilepsy.

CDI cutoff of CDI > 15. Area under the curve (AUC) and its 95% confidence intervals (CI) for the ROC curve were calculated. An AUC of 0.5 indicates no predictive power, whereas an AUC of 1 indicates perfect prediction. Sensitivity, specificity, and positive/negative predictive values, as well as their confidence intervals, were computed. A cutoff point was obtained by selecting the point on the ROC curve that maximized both sensitivity and specificity. The chosen cutoff correctly classified the highest number of individuals and incorrectly classified the least number (thus maximizing both sensitivity and specificity). The ROC analyses for the NDDI-E-Y and the NDDI-E were compared using a nonparametric approach for paired samples; ROC analysis was also separately performed for each item of the NDDI-E-Y.

3. Results

3.1. Sample characteristics

Ninety-seven youths were included. Demographic and clinical data are shown in Table 2.

Mean CDI score was 10.4 (standard deviation [SD] = 7.1). A CDI score > 15 occurred in 21.6% (n = 21/97). Mean CDRS-R score was 31.2 (SD = 13.90). Mean NDDI-E-Y score was 22.0 (SD = 7.4. Concerning the optimal cutoff of 32 defined by Wagner's study, 16/97 (16.5%) patients in our study had an NDDI-E-Y score of 32 or more. Mean NDDI-E score was 10.5 (SD = 5.9).

For item 6 of the NDDI-E-Y "I think about dying or killing myself", 81/97 (83.5%) reported no suicidal ideation, characterized by a score of 1; however, 16/97 (16.5%) reported at least occasional thoughts of suicide in the preceding 2 weeks.

3.2. Internal structural validity

Response distribution for each of the 12 items of the NDDI-E-Y and the 3 items of the NDDI-E is presented in Table 1. Floor effects ranged from 28.9% to 83.5% and ceiling effects from 1% to 12.4%. Item 2, 6, 14, and 15 exhibited the greatest floor effect (proportion of individuals who obtained the lowest ("never") score > 60%).

Correlation between each of the 15 items was analyzed and was high (>0.6) between items 3 and 5, items 3 and 9, items 5 and 9, items 5 and 10, items 6 and 10, and items 6 and 14; see Supplementary materials.

Correlation between items with the overall corrected scores was globally higher than 0.4 (Table 3). All NDDI-E-Y items were significantly and positively associated with the corrected overall NDDI-E-Y score. The lowest scores occurred for items 2, 7, and 8. Cronbach's alpha coefficient was 0.862 and ranged from 0.862 to 0.881 after item removal. None of the items would increase the Cronbach's alpha if deleted (Table 3).

3.3. External validity

Correlation was very high between total NDDI-E-Y and NDDI-E scores (r (97) = 0.901, p < 0.0001), and high between NDDI-E-Y and CDI (r (97) = 0.848, P < 0.0001), and between NDDI-E-Y and CDRS-R (r (97) = 0.724, P < 0.0001).

3.4. Receiver operator characteristics

The ROC analysis of the NDDI-E-Y showed an AUC of 0.967 (95% CI 0.909–0.992), (p < 0.0001). The cutoff point that maximized both sensitivity and specificity was 23. Sensitivity, specificity, and positive and negative predictive values were 100% [83.9; 100], 82.9% [72.5; 90.6], 61.8 [43.6; 77.8], and 100% [94.3; 100], respectively. Mean NDDI-E-Y score in YWE with MDD was 32.42 (SD = 4.87), without MDD 19.13 (SD = 5.04).

The ROC analysis of the 6-item adult NDDI-E showed an AUC of 0.937 (95% CI 0.868–0.976), (p < 0.0001); the cutoff that maximized both sensitivity and specificity was 11. Sensitivity, specificity, and positive and negative predictive values were 95.2% [76.2; 99.9], 85.5% [75.6; 92.5], 64.5 [45.4; 80.8], and 98.5% [91.8; 100], respectively.

Pairwise comparison of ROC curves for NDDI-E-Y and NDDI-E scores was not statistically significant despite a trend (p = 0.07) (z = 1.817); see Supplementary materials.

Each of the 12 items of the NDDI-E-Y and the 3 additional NDDI-E items were also statistically tested (Table 1). All these items exhibited poorer ROC properties than the total score of the NDDI-E-Y and NDDI-E. Scores < 0.8 were seen for items 2, 3, 6, 7, 8, and 12 of the NDDI-E-Y

Table 3
Corrected item-total correlations and Cronbach's alpha if item is deleted from the NDDI-E-Y. Based on results of psychometric testing of each item, items highlighted in gray were retained as the most pertinent and were tested as a short 6-item version of the NDDI-E-Y (see Table 1, Results, and Supplementary material).

	Items	Corrected item-total correlation	Cronbach's alpha if item is deleted
1	Everything is a struggle/Tout est. une lutte	0.558	0.875
2	I have trouble finding anything that makes me happy/J'ai du mal à trouver quoi que ce soit qui me rend heureux	0.445	0.881
3	I feel like crying/J'ai envie de pleurer	0.609	0.872
4	I feel frustrated/Je me sens frustré(e)	0.556	0.875
5	I feel unhappy/Je me sens malheureux (se)	0.788	0.862
6	I think about dying or killing myself/Je pense à mourir ou à me tuer	0.587	0.876
7	Nothing I do is ever right/Je ne fais jamais rien de bien	0.471	0.880
8	I feel sorry about things/Je me sens désolé(e) pour des choses	0.512	0.878
9	I feel sad/Je me sens triste	0.695	0.867
10	I feel guilty/Je me sens coupable	0.723	0.865
11	I feel cranky or irritated/Je me sens grincheux (se) ou irrité(e)	0.546	0.876
12	I feel alone/Je me sens seule	0.559	0.875

and items 13, 14, and 15 (the 3 extra items belonging to the NDDI-E) (see Table 1).

3.5. Supplementary analyses: elimination of items with poorer psychometric properties

We thus analyzed 3 separate aspects of individual item psychometric properties: floor/ceiling effect, correlation between items, and ROC curve. Floor effect was seen for items 2, 6, 14, and 15. In terms of correlation, items 5 and 9 of the NDDI-E-Y ("I feel unhappy"; "I feel sad") had a correlation index > 0.7 and thus appeared redundant. Otherwise item 6 of the NDDI-Y-E ("I think about dying or killing myself") and item 4 of the NDDI-E ("I'd be better off dead") showed a similar degree of correlation, as might be expected. While proposing a shorter version of the NDDI-E-Y was not a main objective of this study, it nonetheless seemed a logical next step to reanalyze instrument properties after eliminating items with poorer psychometric performance. While item 6 pertaining to suicidal ideation was not among those with the strongest properties, it seemed important to retain this, given clinical importance of the symptom and documented usefulness of this item in screening for suicidal ideation [24]. The 6 retained items were as follows: items 1 ("Everything is a struggle"), 4 ("I feel frustrated"), 5 ("I feel unhappy"), 6 ("I think about dying or killing myself"), 9 ("I feel sad"), and 11 ("I feel cranky or irritated") (see Table 1). The ROC analysis of this 6-item short version of the NDDI-E-Y showed an AUC of 0.976 (95% CI 0.923–0.996), ($p < 0.0001$) (Fig. 1). Cutoff point that maximized both sensitivity and specificity for the short 6-item NDDI-E-Y was 12. Sensitivity, specificity, and positive and negative predictive values were 100% [85.5; 100], 85.5% [75.6; 92.5], 65.6 [46.8; 81.4], and 100% [94.5; 100], respectively.

4. Discussion

Our aims were to (1) validate the French version of the NDDI-E-Y and compare its psychometric properties with the original American English version, using equivalent methodology as far as possible; (2) compare performance of the proposed 12-item NDDI-E-Y with the existing 6-item NDDI-E in the same population. The main findings were as follows: (1) significant differences in cutoff of the NDDI-E-Y compared to the original study, which require explanation, and which indicate that the NDDI-E-Y cannot yet be recommended as a global screening tool without further evaluation; (2) that in our population, the NDDI-E-Y did not display statistically significant advantages over the shorter NDDI-E in screening for depressive symptoms in YWE. Moreover, psychometric analysis of each item revealed discrepancies in performance between items, suggesting that a shorter version of the NDDI-E-Y might be equally useful after removing items with poorer psychometric performance.

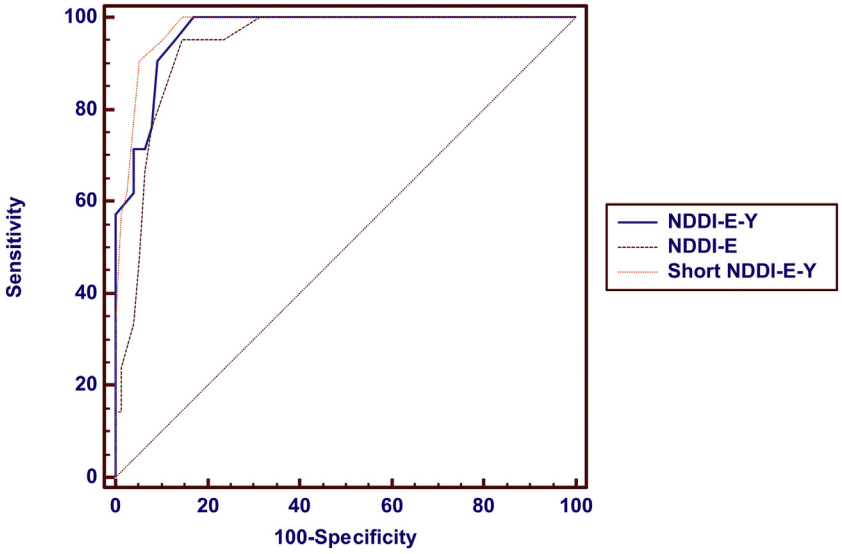

Fig. 1. Comparison of the NDDI-E and NDDI-E-Y and short version of the NDDI-E-Y ROC curves. Despite the pairwise comparison of ROC curves for NDDI-E-Y and NDDI-E, scores were not statistically significant ($p = 0.07$) ($z = 1.817$); pairwise comparison of ROC curves for the short version of the NDDI-E-Y and NDDI-E scores was statistically significant ($p = 0.03$) ($z = 2.101$).

4.1. Clinical similarities between populations

Our population was similar to that reported by Wagner et al. [12] in terms of sample size, average age, age of epilepsy onset, epilepsy duration, and seizure frequency. Our group showed equal distribution of male and female patients (in contrast to Wagner's study that showed female predominance), lower average number of AED, and higher prevalence of symptomatic rather than idiopathic epilepsy. Most importantly, percentages of subjects with possible MDD according to CDI scores were comparable in our population (21.4%) and Wagner's series (25%), and in keeping with previous studies [25,26].

4.2. Choice of validation methodology

Since the CDI-2 (used as the diagnostic gold standard by Wagner et al.) does not exist in French, we used the CDI as the closest alternative; this has good validity and reliability in French youth [4,22,27,28], and is recommended by the French Health Authorities for screening for depression in the pediatric age group [29]. Like the CDI-2, the CDI is not a diagnostic tool but rather a screening instrument for severity of depressive symptoms. Ideally, a structured interview would be preferable for diagnosis of MDD. As such, the choice of the CDI-2 as gold standard in the initial validation study of the NDDI-E-Y has been criticized [30], since it could be argued that comparing one self-reported screening tool to another may imply a suboptimal diagnostic criterion [31]. The same argument applies to the CDI in our study, but this was chosen in order to keep validation methodology as homogenous as possible. In contrast, most validation studies of the adult NDDI-E used the structured Mini International Neuropsychiatric Interview (MINI) as gold standard [15]. A main problem is the lack of an adequate structured interview for use as a gold standard in children with epilepsy; the depression module of the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present (Kiddie-SADS) has been used, but it has been commented that this may not be well-suited to detecting the often atypical presentation of depressive symptomatology in epilepsy [9].

4.3. Discrepancy in cutoff: risk of missing cases of MDD

The NDDI-E-Y validation study by Wagner and colleagues found an optimal cutoff of ≥32 for detection of clinical depressive symptoms, using the CDI-2 as gold standard [12]. On the other hand, we found a markedly lower cutoff of 23. Indeed, 16.5% had an NDDI-E-Y score of 32 or more in our series, representing only 76% of all subjects who were considered to have MDD using the CDI gold standard; that is, almost a quarter of the MDD cases in our series would go undetected if the cutoff of 32 is used. Given similarities in population demographics, methodology, and prevalence of depressive symptoms between both studies, this degree of discrepancy seems surprising. Moreover, it is in marked contrast to multiple validation studies of the adult NDDI-E, which showed a narrow range of cutoff in over 10 different language populations [10,14,15]. Finally, we note that in preliminary testing of an 11-item version of the NDDI-E-Y by the same team, cutoff was 27 [9].

To further evaluate this difference in cutoff, we looked at responses for each item. In 9/12 items of the NDDI-E-Y, mean score in our populations was significantly lower than that of Wagner and colleagues for the same item (using data provided by Dr. Wagner to compare these). While sociocultural differences might play a role [32,33], the similarity of results obtained with other cross-language screening tools between French and American populations [14] and similar prevalence of MDD in both populations tend to argue against significant cultural differences being the main explanation here.

4.4. Development of NDDI-E-Y in children and NDDI-E in adults: different methodological approaches

Recalling methodology of the development of the original adult NDDI-E, discriminant analysis was used to identify a model of 6 items drawn from an original list of 46 items, which offered optimal statistical classification of participants as having MDD or not [34]. This methodology provided a statistically robust base for constructing the NDDI-E, and likely contributed to its subsequent reproducibility as a screening instrument across languages and across cultural groups [14,15]. However, the same methodology was not used for the NDDI-E-Y: this was developed by starting with 14 items (including the 6 items of the NDDI-E, reworded if necessary to improve adolescent comprehension), subsequently reduced to 11 items according to expert discussion but not statistical testing, based upon the responses obtained in a pretest group of 9 healthy youths [9]. Further revisions included deletion of 2 items due to low correlation coefficients, then addition of 3 new items based on expert opinion, leading to the proposed 12-item version [12]. Optimum number and content of items for the NDDI-E-Y were therefore chosen using statistically less rigorous methodology than that of the NDDI-E.

Concerning psychometric properties of individual items, we looked at 3 separate aspects: ROC curve, correlation between items, and floor or ceiling effect, showing marked differences between items. This observation led us to perform supplementary analyses to examine reliability after eliminating more poorly performing items, with retention of 6 items: 1 ("Everything is a struggle"), 4 ("I feel frustrated"), 5 ("I feel unhappy"), 6 ("I think about dying or killing myself"), 9 ("I feel sad"), and 11 ("I feel cranky or irritated"). While proposing a shorter version of the NDDI-E-Y was not a main goal, the ROC analysis for this shorter 6-item version showed superior performance to the 6-item (adult) NDDI-E. Comparison with the 12-item NDDI-E-Y showed a nonsignificant trend to better performance for the shorter 6-item NDDI-E-Y. This suggests that items with poorer psychometric performance may reduce the efficacy of the 12-item NDDI-E-Y. Based on these findings, there is therefore a reasonable basis for proposing a shorter version of the NDDI-E-Y that could be prospectively tested.

4.5. Conclusions

Taken together, the results of the present study indicate that, because of marked discrepancy in cutoff between the 2 populations tested so far, the NDDI-E-Y requires further evaluation before it can be widely recommended as a screening tool for depressive symptoms in YWE. Notably, in terms of robustness as screening instrument, it cannot at present be considered equivalent to the well-established adult NDDI-E, which is recommended for routine screening by the ILAE [8]. Current ILAE recommendations mention the NDDI-E as having been "tailored for use in young people" in the form of the NDDI-E-Y [35]: however, in our view this point deserves to be clarified in order to avoid confusion as to the degree of actual evidence concerning this instrument. In addition, present analyses raise questions about the optimum number and choice of items to achieve efficient yet rapid screening for depressive symptoms in YWE. Future work could examine both validation of the original 12-item NDDI-E-Y and comparison with a shorter, 6-item version. This requires to be performed both in English and in other language versions. Ideally, validation should be performed using a structured interview such as the Kiddie-SADS in addition to CDI or CDI-2, for a more robust gold standard. Further work is urgently required before widespread use of this tool can be recommended; in terms of public health strategies, screening procedures must be conducted in accordance with reliable and accurate cutoff scores, and a screening tool with an overly elevated cutoff score would risk missing cases of MDD.

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Ethical statement

We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Declaration of Competing Interest

None of the authors has any conflict of interest to declare.

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