Epilepsy & Behavior 157 (2024) 109888

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Survey of rehabilitation approaches and plans for individuals with dravet syndrome (RAPIDS) in Italy: Current practices and strategies to progress

Chiara Porto [a,1], Marco Perulli [a,1], Chiara Arpaia [a], Marianna Villa [a], Valentina Arcangeli [a], Michela Quintiliani [a], Maria Luigia Gambardella [a], Carolina Brando [a], Ilaria Contaldo [a], Chiara Veredice [a], Vania Zaghi [b], Giovanna Canepa [b], Simona Borroni [b], Daniela Pia Rosaria Chieffo [a], Domenica Immacolata Battaglia [a,*]

[a] UOC di Neuropsichiatria Infantile, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Roma, Italy
[b] Gruppo Famiglie Dravet APS, Italy

ARTICLE INFO

Keywords:
Dravet syndrome
Rehabilitation
Speech therapy
Physiotherapy
Survey
Families

ABSTRACT

Dravet syndrome, a developmental and epileptic encephalopathy, manifests with varying degrees of cognitive and communication impairment, postural and movement disorders (such as ataxia, coordination issues, and crouch gait) and behavioural challenges (including attention deficit/hyperactivity, oppositional/defiant behaviour, and autistic traits). Rehabilitation is a valuable tool for most patients, typically prescribed to address the most pressing issues. However, current practices often fall short in proactively preventing and treating known challenges associated with the syndrome, as indicated by the latest literature, at different life stages. Furthermore, there is a notable lack of evidence regarding treatment types and efficacy specific to people with Dravet Syndrome.

Conducted in collaboration with one of the Italian Patient associations, this national survey provides a comprehensive view of the rehabilitation landscape in Dravet Syndrome, as perceived by caregivers. It outlines the types of treatments for 51 patients, based on age and relevant clinical features. The findings reveal a heterogenous rehabilitation approach, only partly tailored to the presence of specific comorbidities, and underline numerous unmet needs. Compared to the past there is indirect evidence that more patients are offered early rehabilitation. Nonetheless, while nowadays speech therapy and neuropsychomotor therapy are nearly universal for children up to the age of 10, some begin physiotherapy and psychotherapy thereafter, with a majority discontinuing treatments. Therefore, families of adolescent and adult patients often face a lack of comprehensive support, predominantly offered when epilepsy is more challenging to control affecting rehabilitation adherence and effectiveness. Finally, a negligible minority is offered treatments such as neurovisual training, augmentative and alternative communication, and occupational therapy. Many of these considerations could apply to other developmental and epileptic encephalopathy with lifelong disability. This survey calls for more data collection on this important topic for more efficient allocation of rehabilitation resources.

1. Introduction

Dravet syndrome (DS), the most common genetic epilepsy syndrome, affects 1 in 16 000 live births[1]. Initially described by Charlotte Dravet in 1978 as “Severe myoclonic epilepsy in infancy”, DS is characterized by early onset drug-resistant epilepsy, followed by cognitive, motor, sleep, speech and behavioral disorders.

Despite clinical heterogeneity, certain neurocognitive and behavioral issues prevail in the syndrome and were included in the characteristic features since the first clinical description[2]. Moreover, these issues represent the most relevant contributors to a negative impact on quality of life[3–5].

Visual attention and hand-eye cohordination deficits are the mostearly issues highlighted by neurodevelopmental tests[6,7], visuomotor and visuospatial competences continue to be a relative weakness in adolescence[8]. Language is also affected with a predominance of

* Corresponding authors.
E-mail address: domenicaimmacolata.battaglia@unicatt.it (D.I. Battaglia).
[1] These authors contribuited equally to this work

https://doi.org/10.1016/j.yebeh.2024.109888
Received 22 February 2024; Received in revised form 2 June 2024; Accepted 8 June 2024
Available online 10 July 2024

phonological deficits and dysarthria in contrast to relatively spared comprehension skills[9,10].

A narrative review in 2016[11] proposed the hypothesis of an original neuropsychological phenotype in Dravet syndrome, consisting of a defect in sensorimotor integration, particularly of visuoconstructive abilities, which is already evident in the first years of life.

Numerous studies have confirmed the presence of developmental delay with slowing of psychomotor milestones acquisition after the second year of life[12]. Intellectual disability of varying degrees is evident later in life in nearly all patients[13] and is included in the criteria of the latest ILAE revision of epilepsy syndromes during the disease course[14]. Moderate to severe impairment in intellectual and adaptive behavior predominates the adult life[15,16].

Moreover, parents state that their burden of care is greatly affected by behavioural disorders[17]. These can be of varying degrees and include attention deficit/hyperactivity disorder, oppositional/defiant disorder, obsessive–compulsive disorder and autistic spectrum disorder. A systematic review in 2020 found that the prevalence of behaviour disorders on standardized instruments ranged from 43 to 100 %[18]. Attention deficits are more reported in early childhood and among school-aged children but were never assessed longitudinally. In a multicentric prospective longitudinal study[12] a high prevalence of behavioural disorders was found in pre-school children followed since seizure onset and evaluated through parental reports and direct observations. In particular, attention disorders were noted in 29/32 (90,6%), hyperactive disorders in 20/32 (62,5%) and oppositional disorder in 10/32 (31,3%). A lower prevalence was recently reported in the Italian registry on DS (RESIDRAS) and other phenotypes related to SCN1A mutations: oppositional traits in 7/55 (12,7%), attention deficit in 26/55 (47.3 %) and autism spectrum symptoms in 8/55 (14.5 %)[19]. These differences can be attributed to different age at assessment and different instruments used.

Motor developmental milestones are generally preserved in the first year with onset of motor symptoms typically noted afterwards but often standardized assessments are lacking. A 2019 systematic review describes a diverse range of gait alterations observed in individuals with DS, the most frequent being crouch gait in half of 93 patients, with an age range from 2,5 to 47 years[20]. Crouch gait is a sagittal plane deviation characterized by excessive ankle dorsiflexion, along with excessive hip and knee flexion during the stance phase. Crouch gait in DS compared to that seen in spastic diplegic cerebral palsy is characterized by smaller contractures at the hip and knee[21]. Parkinsonian and cerebellar features are also frequently reported[22] but their prevalence is difficult to estimate due to inconsistencies in definitions and assessments performed. The evolution of the motor disorder throughout development is not yet well understood, however, a progressive deterioration of gait from the second decade of life was described by some authors[21], with significant impact on mobility and self-autonomy.

There are several studies in the literature focused on the pharmacological approach to the treatment of seizures. Although some recently adopted drugs promise to improve cognitive, motor, and behavioral deficits[23] they were approved based on their efficacy on seizures and assessment of outcomes beyond seizure controls are still lacking.

In this landscape, despite rehabilitation is still the main hope for improvement in cognitive, motor, and behavioral deficits, rehabilitation plans are little discussed and analyzed in the scientific community dealing with DS. In 2015, a prospective study[24] applied a targeted rehabilitation program to young adults with epilepsy and intellectual disability, documenting a moderate improvement in quality of life (QoL) and independence. Recent evidence suggest that physical exercise also contributes to improvements in psychosocial dimensions and comorbidities in patients with epilepsy, increasing quality of life[25].

In DS, there is a notable absence of a comprehensive characterization of comorbidities across the lifespan, with specific gaps in recognizing and systematically preventing issues faced in adulthood. Moreover, data is lacking regarding the effectiveness of the rehabilitation approaches used at different ages to address the aforementioned comorbidities.

2. Objective

The aim of this national survey is to describe the prevalence of comorbidities in DS them throughout the lifespan as perceived by families. Moreover, we want to assess Rehabilitation Approaches and Plans for Individuals with Dravet Syndrome (RAPIDS) in Italy. The ultimate goal is to define standards of care for prevention and treatment of comorbidities to promote autonomies and quality of life of individuals with DS.

3. Materials and methods

The survey received support from "*Gruppo Famiglie Dravet APS*", an association of patient's families which distributed the survey link (https://it.surveymonkey.com) to all 174 contacts within the network of families. The survey follows a mixed cross-sectional and retrospective longitudinal design.

To comply with the General Regulations on data protection (GDPR) regarding sensitive personal data processing, respondent anonymity was rigorously maintained. Data collection took place from the 1st of August to the 30th of October 2019. A total of 88 respondents participated, with 51 providing answers related to rehabilitation. Thirty-seven questionnaires were excluded due to excessive missing data, partial, or incongruent answers. Individual anonymized data were exported into an "Excel" worksheet, and descriptive statistical measures were computed.

The anonymous questionnaire (Appendix 1) included the following items:

- Demographic background (sex, age, geographic origin, family members)
- Genetic mutation (deletion, missense mutation, no mutation, splicing, truncating mutation of SCN1A gene)
- Type of seizures at the time of the survey (focal, generalized tonic-clonic, atonic, absence)
- Pharmacological treatment at the time of the survey
- Clinical features other than seizures at the time of the survey
- Neuromotor disorders (gait disturbances, balance/ataxia disorders)
- Speech disorders (verbal/nonverbal patients; expressive and comprehension difficulties)
- Neurovisual disorders
- Intellectual disability (mild/severe/moderate)
- Behavioral disorders (repetitive behaviors, oppositional defiance, autistic traits, aggressivity, attention-deficit/hyperactivity disorder)
- Attendance at sports and other group activities at the time of the survey
- Type of rehabilitation performed at the time of the survey (2019) and retrospectively at different age periods (0–5 years; 6–10 years; 11–14 years; 15–19 years; over 20 years). Options included:
- Neuropsychomotor therapy: an integrated therapy working on motor, cognitive and behavioral skills, widely available in Italy.
- Speech therapy
- Augmentative and Alternative Communication (AAC)
- Physiotherapy
- Applied Behavior Analysis (ABA)
- Cognitive-behavioral psychotherapy
- Feurstein method
- Hydrokinesiotherapy
- Neurovisual training
- Occupational therapy

Descriptive statistics were employed to summarize the key features of the dataset, providing an overview of the central tendencies, variability, and distribution of the collected data.

4. Results

4.1. Population description

4.1.1. Demographic data

The analysis included 51 questionnaires from patients exhibiting a balanced gender ratio (27/51 females, 52,9%) and encompassing a broad age range, with a median age of 13 years (IQR 10–18 years, min 2 years, max 42 years) (Fig. 1).

The geographical distribution of patients is depicted in Fig. 1. The majority, 56,8% (29/51), is located in northern Italy, with the remaining 31,4% (16/51) in central and 11,8% (6/51) in southern Italy. Regions with more responders are Emilia Romagna (n = 11), followed by Lombardia (n = 8), Lazio (n = 7) and Tuscana (n = 5). No data was available from Sardegna, Calabria, Basilicata, Molise, Valle d'Aosta and, Trentino-Alto Adige.

4.1.2. Epilepsy

The most common seizure type at the time of the survey was generalized tonic-clonic (GTC) in 61 % of cases, followed by focal (51 %), myoclonus (43 %), absences (25 %) and atonic seizures (4 %). Almost all patients are on polytherapy (94 %) while 3 patients (6 %) were taking only one antiseizure medication.

4.1.3. Non-seizure clinical features

4.1.3.1. Neuromotor disorders. Gait impairment, including issues like lack of balance or decreased speed was reported by families in 36 out of 51 patients (70,6%). Patients experiencing gait impairment had a median age of 13 years. Furthermore, dysarthria was observed in 51 % of patients (26/51), at a median age of 13 years, and dysphagia in 27 % of the sample (14/51), at a median age of 15 years.

4.1.3.2. Behavioural disorders. Behavioural disorders were reported by families with the following prevalence:

- Attention deficit hyperactivity disorder in 86,3% (44/51)
- Repetitive behavior in 74,5% (38/51)
- Oppositional defiant in 76,5% (39/51)
- Autistic traits in 45,1% (23/51)
- Aggressiveness in 27,5% (14/51)

Looking at the prevalence according to age groups (Fig. 2), most behavioural issues have an early onset and are still prevalent in adolescence and adult age.

4.1.3.3. Language, neurovisual and neuropsychological disorders. In terms of language skills, 86,3% (44/51) were verbal and 13,7% (7/51) non-verbal.

A language impairment was perceived by 88,2% (46/51) of the caregivers.

Some degree of cognitive impairment was reported by all families. In the majority of responses it was classified as moderate (54.9 %, 28/51 patients), followed by severe (29,4%, 15/51 patients) and mild in only 15,7% (8/51 patients). Patients with mild cognitive impairment had a median age of 13 year, in line with the age distribution of this cohort.

The neurovisual function was evaluated in 29 patients and 12 of them were found to have additional neurovisual deficit to that expected from their intellectual functioning.

4.2. Interventions

4.2.1. Attendance at sports activities and aggregate groups

In the sample under study, 29.4 % (15/51) participate in sports, in particular more participation is described by patients between 11 and 14 years old (40 % of the cohort, 6/15). In the over 20 s, 30 % of patients participate in sports (3/10), with a predilection for soccer, athletics and gym. Only 4 out of 51 patients (8 %) attend other group activities.

4.2.2. Rehabilitation

Cross-sectional analysis of the data, in the age-related view, revealed that all children under the age of 10 years practiced some rehabilitation therapy while the proportion decreased gradually over time reaching 40 % (4/10) in the over 20 s (Fig. 3).

At the time of the Survey, 14/14 patients under 10 years old (100 %) practice neuropsychomotor therapy and 13/14 (93 %) of them practice speech therapy.

In patients between 11 and 14 years of age, the most frequent

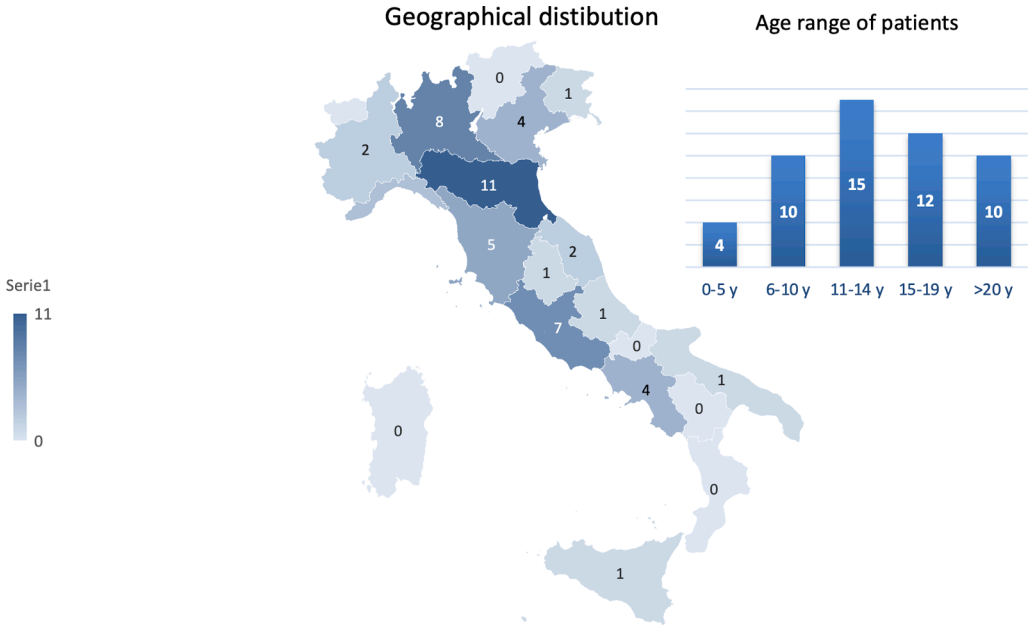

Fig. 1. The median age of the patients is 13 years, with an interquartile range (IQR) of 10–18 years. In terms of geographical distribution, 56.8 % of the patients are located in northern Italy, 31.4 % in central Italy, and 11.8 % in southern Italy.

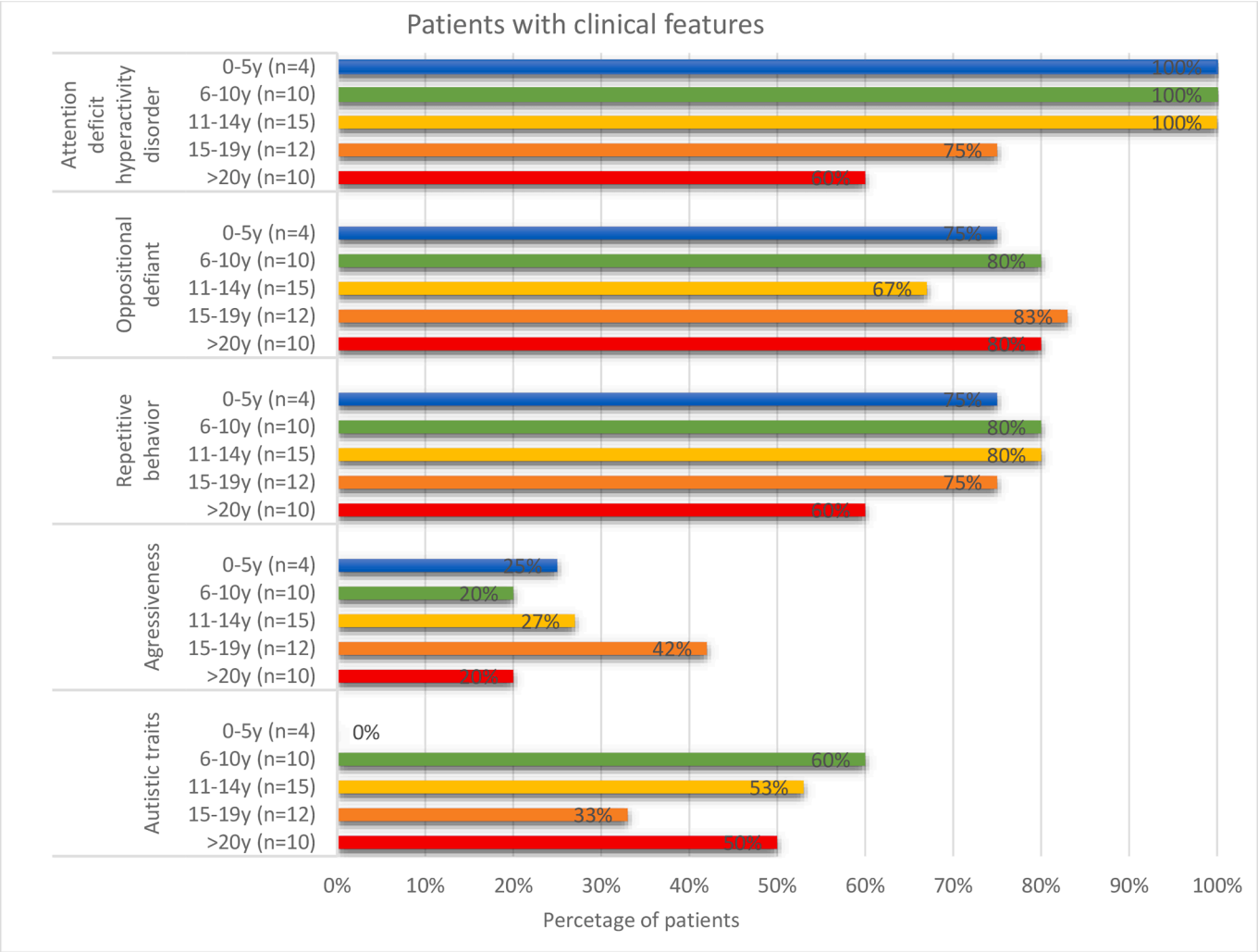

Fig. 2. The frequency of behavioral disorders described by families shows a high prevalence of Attention deficit hyperactivity disorder, followed by repetitive and oppositional behaviors. These behavioral issues tend to appear early and persist into adolescence and adulthood.

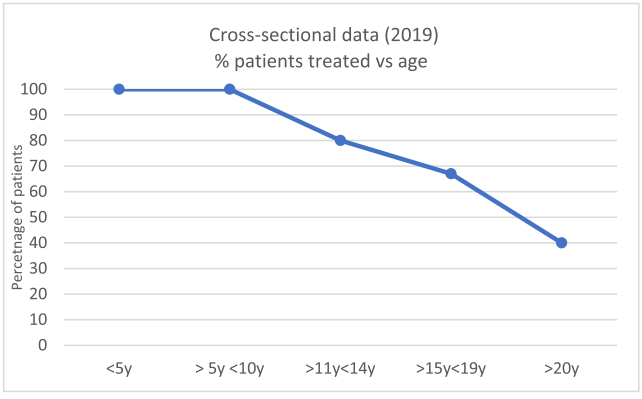

Fig. 3. Cross-sectional data showing that most children under 10 years old undergo rehabilitation therapy, with the percentage decreasing as they grow older.

rehabilitation therapy is speech therapy, practiced by 7/15 (47 % of patients), followed by psychotherapy practiced by 6/15 patients (40 %). In this age group, 13 % of the cohort (2/15) practice physiotherapy and 13 % occupational therapy (2/15).

In patients aged between 15 and 19 at the time of data collection, 6/12 patients (50 %) practiced physiotherapy, 5/12 patients (42 %) occupational therapy and 6/12 patients (50 %) psychotherapy.

Adult patients practiced mostly physiotherapy (4/10), coupled with hydrokinesiotherapy in 2/10 and speech therapy in 1/10. Most patients (6/10, 60 %) stopped all rehabilitation.

Looking at retrospective data (Fig. 4), 90,2% (46/51 patients) received neuropsychomotor therapy and 70,6% (36/51) underwent speech therapy during their life. AAC was utilized in 31,4% (16/51) of patients.

Physiotherapy was carried out in 41,2% (21/51) of cases, particularly in the second decade of life (6/21). Hydrokinesitherapy was employed in 25,5% (13/51) of cases.

The cognitive-behavioural therapy was performed in 27,5% (14/51) of patients, occupational therapy in 17,6% (9/51), neurovisual training in 7,8% (4/51), ABA and the Feurstein method in 3,9 % (2/51).

If we look at the proportion of patients who were offered rehabilitation at different times of their life (Fig. 5) we can see that patients under 10 years are increasedly offered therapy. In fact, while all patients in this age group were offered some therapy after 2014, in 2000–2004 more than one third of patients was not performing any therapy. The same increase is not seen in the adolescents which are out of rehabilitation in a similar proportion over time. The type of rehabilitative treatment carried out by the sample under study as they grow up is illustrated in Fig. 4.

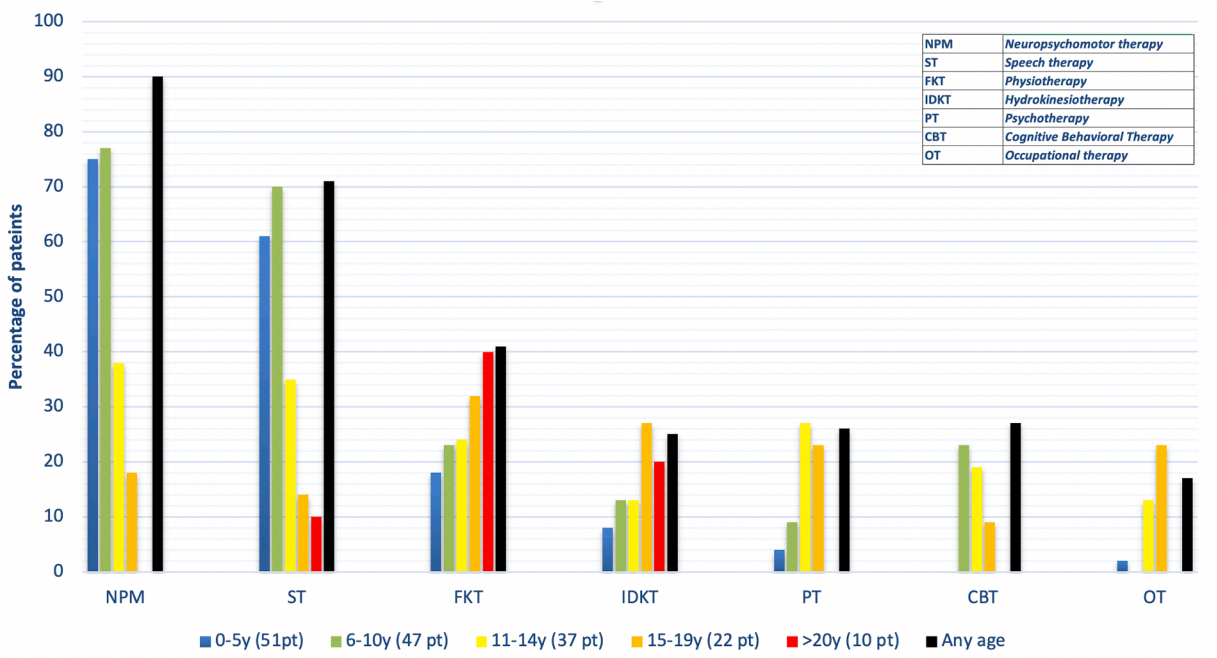

Fig. 4. The rehabilitative therapy types performed by the sample under study are categorized by age group and reported here.

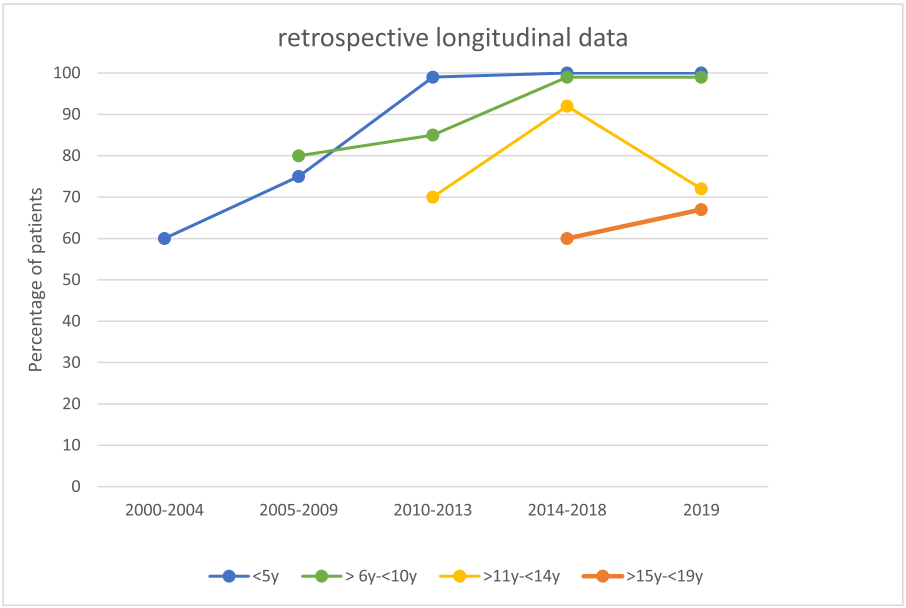

Fig. 5. Evaluating retrospective data from 2000 to 2019, it is evident that the percentage of patients under the age of 10 who were offered therapy increased over time. This trend is not observed among adolescents, as a similar percentage of them remain out of rehabilitation over time.

5. Discussion

To the best of our knowledge, this study represents the first attempt to evaluate the types of rehabilitation therapies provided to both children and adults with Dravet Syndrome (DS), emphasizing age-related variations in clinical features and corresponding treatment. In this national survey, we gathered data from families of patients associated with "Gruppo Famiglie Dravet Associazione ONLUS" residing in Italy.

The collected data pertain to the immediate pre-pandemic period of COVID-19 and therefore may reflect an approach that gradually came back to practice but be partly changed after the forced lockdown. Survey participation was more pronounced among families residing in the North, while lower participation was observed among those residing in the South. This discrepancy may be attributed to reduced engagement with patient family associations of the latter. The respondents exhibit significant heterogeneity in age, with a notable proportion representing adult patients. This is particularly significant due to the distinct clinical features present in adults, as well as their reference to different rehabilitation services.

The prevalence of various clinical features generally aligns with the literature. Gait problems, dysarthria and dysphagia were reported in similar proportion to that presented in other surveys[26]. In our survey dysphagia was the only issue seen more frequently in older patients. Issues with feeding are highly prevalent in DS and seen in almost all patients, as recently described in one of the largest surveys of comorbidities in children with DS related to 202 patients [26] A recent case-

report describes the history of a young adult with new onset dysphagia who needed percutaneous endoscopic gastrostomy (PEG) insertion at the age of 21 after a progressive weight loss, accompanied by issues of dehydratation and drug compliance[27]. The same paper cites unpublished data of PEG insertions in 20 % of 50 adults with DS followed at that center. Nonetheless this issue has received little attention in terms of structured evaluations and rehabilitation therapy. At the time of our survey only 4 out of 30 patients aged 15 or above were doing speech therapy, which can effectively assess and may improve the ability to chew and swallow[28].

Given the high prevalence of cognitive and language impairment together with autistic features a more widespread use of AAC would be expected. In fact, AAC has been shown to be effective in improving communication, daily living skills, and socialization in individuals with severe intellectual disabilities[29] and is part of the standard of care provided to children with autism spectrum disorder[30]. Nonetheless this was recently shown to be an underutilized approach in common practice[31].

In terms of behavioral issues, our survey is in line with the literature citing attention as the most common problem in more than 4 subject out of 5. Here, compared to other reports[32], families cited more frequently issues with repetitive and oppositional behavior, both affecting about three quarters of our sample. This may be due to the fact that the median age of our population was 13 years, significantly older than the mean age often reported in large literature cohorts. In fact, these issues were recently shown to be more relevant in adolescents and young adults[13]. Despite high rates of autistic traits and problematic behaviors, only a small minority of patients were offered cognitive-behavioral therapy, with a peak of 19 % in adolescence when most of this issues peak in incidence. Application of early behavioral interventions allows a significant reduction in problem behaviors [33,34] and an increase in communication and other appropriate behaviors in both patients with autism spectrum disorders and with intellectual and developmental disabilities [35,36]. According to our analysis, the percentage of patients implementing specific strategies such as ABA. is still very low.

In almost half of the patients undergoing specific neurovisual assessment an impairment beyond that expected from cognitive function was found, but more than one third of the cohort did not perform any assessments. Vision in DS was found to be impaired particularly regarding motion perception (dorsal stream vulnerability) in five patients[37] but this exploratory result was never replicated in larger cohorts nor controlled for cognitive skills. There is limited evidence that early interventions can improve visual functions in patients with Down Syndrome[38] Based on our clinical experience with DS, we observe that the impact of visual impairment in DS is currently underestimated and is rarely integrated in rehabilitation strategies. Furthermore, it is rarely taken into account when providing parent training for environmental enrichment.

Looking at longitudinal retrospective data we show that patients who are now adult were offered therapy less often compared to those that are children nowadays. The same trend is not seen for treatment in adolescence although this refers to more recent times. This is in line with our experience with patients being diagnosed earlier with consequent earlier access to treatment but with a relative reduction of services for adolescents and young adults.

Adolescence represents a pivotal period for achieving self-sufficiency, therefore, enhancing care for individuals in this age group would not only improve the quality of life for patients and their families, but also alleviate the burden of care on both society and caregivers, along with associated indirect costs. Strategies for increasing autonomy can be identified according to each patient's needs through occupational therapy, attended by a minority of patients in this age group. Numerous studies support the use of occupational therapy for adult patients with intellectual disabilities, employing traditional approaches as well as technology training and caregiver support, to enhance their occupational performance[39].

Despite the many types of rehabilitative interventions available, it is not possible to favor one over another due to the absence of comparative studies. However, as already demonstrated for other rare genetic syndromes [40], each therapy evaluated individually shows some level of effectiveness, so a comprehensive approach to rehabilitation interventions could improve function and quality of life. To this end, personal factors that characterize everyone play a fundamental role in assessing the patient's function when planning rehabilitation. Conducting a preliminary assessment of these factors in the rehabilitation process allows therapy to be targeted to the patient's specific needs and improves individual compliance by enhancing motivation [41].

Finally, only about one third of the group practiced sports or had the chance to be involved in group activities with peers. Regular physical activity can improve the outcome of patients with neurological disorders such as epilepsy: reducing proinflammatory markers and critical manifestations, promoting socialization, reducing anxiety states and improving mood[42]. Engaging in such activities might be hindered by motor difficulties, oppositional behaviors and concerns about potential seizure triggers or acute seizure management. Given the potential benefits associated with these activities[43] it is essential for those planning rehabilitation of DS to reduce these barriers and promote integration in social and recreation activities that might be the first step toward work inclusion and increased self-sufficiency.

Our study has limitations, some of whom are valid for all surveys: questions can be misunderstood by responders who cannot be supported by clinicians and answers are based on the caregivers perception and memory. The advantage is low risk of conditioning and the possibility to reach a wider public, representative of the national panorama.

With regards to this specific survey, a relative limitation is the sample size, which was sufficient to draw a qualitative picture but insufficient for solid statistical analysis. There is a relative lack of responses from southern Italy and islands which may imply the results are not generalizable to that geographical area. Moreover, only a part of those reached by the questionnaire completed it, maybe in part due to its length. The incompleteness of the provided answers hinders the assessment of caregivers' perception regarding the effectiveness of rehabilitation therapy and other data part of the original questionnaire. Finally, our considerations on the evolution on treatment offered over time is limited by the retrospective nature of the survey and the heterogeneity of patients ages and will have to be confirmed by larger and ideally prospective studies.

6. Conclusions

In conclusion, this survey marks the first attempt to evaluate rehabilitation therapies for individuals with Dravet Syndrome (DS) in Italy. It reveals a relative undertreatment, particularly after puberty, of behavioral issues, autism, dysphagia, visual and gait problems compared to their actual incidence. A negligible minority is offered treatments such as neurovisual training, AAC, and occupational therapy. Participation in sports and activities with peers is relatively low. Therefore, the development of guidelines for Rehabilitation Approaches and Plans for Individuals with Dravet Syndrome (RAPIDS), informed by current evidence on the natural history and comorbidities of DS, is essential to increase autonomies and quality of life to reduce the burden of care for families and caregivers.

Larger studies with improved geographical representation, involving subjects of different ages and degrees of cognitive impairment, are warranted to validate these initial findings and shape informed health policies. International studies will allow for the comparison of the performance of our national healthcare system in comparison to that of other countries.

CRediT authorship contribution statement

Chiara Porto: Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Marco Perulli:** Writing – review & editing, Writing – original draft, Data curation. **Chiara Arpaia:** Writing – review & editing, Data curation. **Marianna Villa:** Writing – review & editing, Data curation. **Valentina Arcangeli:** Writing – review & editing, Conceptualization. **Michela Quintiliani:** Writing – review & editing, Conceptualization. **Maria Luigia Gambardella:** Writing – review & editing. **Carolina Brando:** Writing – review & editing, Formal analysis, Data curation. **Ilaria Contaldo:** Writing – review & editing. **Chiara Veredice:** Writing – review & editing. **Vania Zaghi:** Writing – review & editing, Conceptualization. **Giovanna Canepa:** Writing – review & editing, Conceptualization. **Simona Borroni:** Writing – review & editing, Conceptualization. **Daniela Pia Rosaria Chieffo:** Writing – review & editing, Conceptualization. **Domenica Immacolata Battaglia:** Writing – review & editing, Supervision, Methodology, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2024.109888.

References

[1] Wu YW, Sullivan J, McDaniel SS, et al. Incidence of dravet syndrome in a US population. Pediatrics 2015;136(5):e1310–5. https://doi.org/10.1542/peds.2015-1807.

[2] Dravet C. Les epilepsies graves de l'enfant. Vie Medicale 1978;8:543–8.

[3] Brunklaus A, Dorris L, Zuberi SM. Comorbidities and predictors of health-related quality of life in Dravet syndrome. Epilepsia 2011;52(8):1476–82. https://doi.org/10.1111/j.1528-1167.2011.03129.x.

[4] Sinoo C, de Lange IML, Westers P, Gunning WB, Jongmans MJ, Brilstra EH. Behavior problems and health-related quality of life in Dravet syndrome. Epilepsy Behav 2019;90:217–27. https://doi.org/10.1016/j.yebeh.2018.11.029.

[5] Makiello P, Feng T, Dunwoody B, et al. Comorbidities and predictors of health-related quality of life in Dravet syndrome: A 10-year, prospective follow-up study. Epilepsia 2023;64(4):1012–20. https://doi.org/10.1111/epi.17531.

[6] Villeneuve N, Laguitton V, Viellard M, et al. Cognitive and adaptive evaluation of 21 consecutive patients with Dravet syndrome. Epilepsy Behav 2014;31:143–8. https://doi.org/10.1016/j.yebeh.2013.11.021.

[7] Reilly C, Bjurulf B, Hallböök T. Intellectual functioning and adaptive behaviour in children with Dravet syndrome: A population-based study. Dev Med Child Neurol 2023;65(6):831–7. https://doi.org/10.1111/dmcn.15495.

[8] Olivieri G, Battaglia D, Chieffo D, Rubbino R, Ranalli D, Contaldo I, et al. Cognitive-behavioral profiles in teenagers with Dravet syndrome. Brain and Development 2016 Jun;38(6):554–62. https://doi.org/10.1016/j.braindev.2015.12.014. Epub 2016 Jan 18 PMID: 26797655.

[9] Turner SJ, Brown A, Arpone M, Anderson V, Morgan AT, Scheffer IE. Dysarthria and broader motor speech deficits in Dravet syndrome. Neurology 2017;88(8):743–9. https://doi.org/10.1212/WNL.0000000000003635.

[10] Chieffo D, Battaglia D, Lucibello S, Gambardella ML, Moriconi F, Ferrantini G, et al. Disorders of early language development in Dravet syndrome. Epilepsy Behav 2016 Jan;54:30–3. https://doi.org/10.1016/j.yebeh.2015.10.027. Epub 2015 Nov 26 PMID: 26630186.

[11] Battaglia D, Ricci D, Chieffo D, Guzzetta F. Outlining a core neuropsychological phenotype for Dravet syndrome. Epilepsy Res 2016;120:91–7. https://doi.org/10.1016/j.eplepsyres.2015.11.020.

[12] Battaglia D, Chieffo D, Lucibello S, et al. Multicenter prospective longitudinal study in 34 patients with Dravet syndrome: Neuropsychological development in the first six years of life. Brain and Development 2021;43(3):419–30. https://doi.org/10.1016/j.braindev.2020.10.004.

[13] Feng T, Makiello P, Dunwoody B, et al. Long-term predictors of developmental outcome and disease burden in SCN1A -positive Dravet syndrome. Brain Commun 2024;6(1):1–10. https://doi.org/10.1093/braincomms/fcae004.

[14] Zuberi SM, Wirrell E, Yozawitz E, et al. ILAE classification and definition of epilepsy syndromes with onset in neonates and infants: Position statement by the ILAE Task Force on Nosology and Definitions. Epilepsia 2022;(March):1349–1397.. https://doi.org/10.1111/epi.17239.

[15] Darra F, Battaglia D, Dravet C, et al. Dravet syndrome: Early electroclinical findings and long-term outcome in adolescents and adults. Epilepsia 2019;60(S3):S49–58. https://doi.org/10.1111/epi.16297.

[16] Lo Barco T, Offredi F, Castino E, et al. Adaptive behaviour in adolescents and adults with Dravet syndrome. Dev Med Child Neurol 2023;65(6):838–46. https://doi.org/10.1111/dmcn.15448.

[17] Postma A, Milota M, Jongmans MJ, Brilstra EH, Zinkstok JR. Challenging behavior in children and adolescents with Dravet syndrome: Exploring the lived experiences of parents. Epilepsy Behav 2023;138:108978. https://doi.org/10.1016/j.yebeh.2022.108978.

[18] Jansson JS, Hallböök T, Reilly C. Intellectual functioning and behavior in Dravet syndrome: A systematic review. Epilepsy Behav 2020;108. https://doi.org/10.1016/j.yebeh.2020.107079.

[19] Balestrini S, Doccini V, Giometto S, et al. A registry for Dravet syndrome : The Italian experience August 2022;2023:1–18. https://doi.org/10.1002/epi4.12730.

[20] Wyers L, Van de Walle P, Hoornweg A, et al. Gait deviations in patients with dravet syndrome: A systematic review. Eur J Paediatr Neurol 2019;23(3):357–67. https://doi.org/10.1016/j.ejpn.2019.03.003.

[21] Rodda JM, Scheffer IE, McMahon JM, Berkovic SF, Graham HK. Progressive gait deterioration in adolescents with Dravet syndrome. Arch Neurol 2012;69(7):873–8. https://doi.org/10.1001/archneurol.2011.3275.

[22] Aljaafari D, Fasano A, Nascimento A, Lang AE, Andrade DM. Adult motor phenotype differentiates Dravet syndrome from Lennox-Gastaut syndrome and links SCN1A to early onset parkinsonian features. *Epilepsia.* Published online 2017:1-5. 10.1111/epi.13692.

[23] Strzelczyk A, Schubert-Bast S. Therapeutic advances in Dravet syndrome: a targeted literature review. Expert Rev Neurother 2020;20(10):1065–80. https://doi.org/10.1080/14737175.2020.1801423.

[24] Endermann M. Rehabilitation for young adults with epilepsy and mild intellectual disabilities: Results of a prospective study with repeated measurements. Seizure 2015;26:72–80. https://doi.org/10.1016/j.seizure.2015.02.002.

[25] Duñabeitia I, Bidaurrazaga-Letona I, Diz JC, Colon-Leira S, García-Fresneda A, Ayán C. Effects of physical exercise in people with epilepsy: A systematic review and meta-analysis. Epilepsy Behav 2022;137. https://doi.org/10.1016/j.yebeh.2022.108959.

[26] Knupp KG, Scarbro S, Wilkening G, Juarez-Colunga E, Kempe A, Dempsey A. Parental Perception of Comorbidities in Children With Dravet Syndrome. Pediatr Neurol 2017;76:60–5. https://doi.org/10.1016/j.pediatrneurol.2017.06.008.

[27] Clayton LM, Williams E, Balestrini S, Sisodiya SM. Case report: Dravet syndrome, feeding difficulties and gastrostomy. Front Neurol 2022;13(1). https://doi.org/10.3389/fneur.2022.993906.

[28] Kleinert JO. Pediatric Feeding Disorders and Severe Developmental Disabilities. Semin Speech Lang 2017 Apr;38(2):116–25. https://doi.org/10.1055/s-0037-1599109. Epub 2017 Mar 21 PMID: 28324901.

[29] Uliano D, Falciglia G, Del Viscio C, Picelli A, Gandolfi M, Passarella A. Augmentative and alternative communication in adolescents with severe intellectual disability: a clinical experience. Eur J Phys Rehabil Med 2010 Jun;46(2):147–52. Epub 2010 Apr 13 PMID: 20485219.

[30] Lai MC, Anagnostou E, Wiznitzer M, Allison C, Baron-Cohen S. Evidence-based support for autistic people across the lifespan: maximising potential, minimising barriers, and optimising the person-environment fit. Lancet Neurol 2020 May;19(5):434–51. https://doi.org/10.1016/S1474-4422(20)30034-X. Epub 2020 Mar 3 PMID: 32142628.

[31] Lillehaug HA, Klevberg GL, Stadskleiv K. Provision of augmentative and alternative communication interventions to Norwegian preschool children with cerebral palsy: are the right children receiving interventions? Augment Altern Commun 2023 Dec;39(4):219–29. https://doi.org/10.1080/07434618.2023.2212068. Epub 2023 May 22 PMID: 37212772.

[32] Li BM, Liu XR, Yi YH, et al. Autism in Dravet syndrome: Prevalence, features, and relationship to the clinical characteristics of epilepsy and mental retardation. Epilepsy Behav 2011;21(3):291–5. https://doi.org/10.1016/j.yebeh.2011.04.060.

[33] Brosnan J, Healy O. A review of behavioral interventions for the treatment of aggression in individuals with developmental disabilities. Res Dev Disabil 2011;32(2):437–46. https://doi.org/10.1016/j.ridd.2010.12.023.

[34] Doehring P, Reichow B, Palka T, Phillips C, Hagopian L. Behavioral approaches to managing severe problem behaviors in children with autism spectrum and related developmental disorders: a descriptive analysis. Child Adolesc Psychiatr Clin N Am 2014 Jan;23(1):25–40. https://doi.org/10.1016/j.chc.2013.08.001. Epub 2013 Oct 6 PMID: 24231165.

[35] Kurtz PF, Leoni M, Hagopian LP. Behavioral approaches to assessment and early intervention for severe problem behavior in intellectual and developmental disabilities. Pediatr Clin North Am. 2020;67(3):499–511. https://doi.org/10.1016/j.pcl.2020.02.005. Epub 2020 May 4. PMID: 32443989; PMCID: PMC8018516.

[36] Orim MA, Orim SO, Adeleke PO, Essien EE, Olayi JE, Essien CK, et al. Cognitive behavioral therapy as treatment intervention for aggressive behaviors in clients with intellectual disabilities and concomitant mental health conditions. J Educ Health Promot 2022;11(1):395. https://doi.org/10.4103/jehp.jehp_545_22. PMID: 36824399; PMCID: PMC9942128.

[37] Ricci D, Chieffo D, Battaglia D, et al. A prospective longitudinal study on visuo-cognitive development in Dravet syndrome: Is there a "dorsal stream vulnerability"? Epilepsy Res 2015;109(1):57–64. https://doi.org/10.1016/j.eplepsyres.2014.10.009.

[38] Purpura G, Tinelli F, Bargagna S, Bozza M, Bastiani L, Cioni G. Effect of early multisensory massage interven- tion on visual function in infants with Down syndrome. Early Hum Dev 2014;90:809–13.

[39] Blaskowitz MG, Johnson KR, Bergfelt T, Mahoney WJ. Evidence to inform occupational therapy intervention with adults with intellectual disability: A scoping review. Am J Occup Ther 2021;75(3):7503180010. https://doi.org/10.5014/ajot.2021.043562.
[40] Sommese M, Corrado B. A comprehensive approach to rehabilitation interventions in patients with angelman syndrome: A systematic review of the literature. Neurol Int. 2021;13(3):359–70. https://doi.org/10.3390/neurolint13030036.
[41] Karhula M, Saukkonen S, Xiong E, Kinnunen A, Heiskanen T, Anttila H. ICF personal factors strengthen commitment to person-centered rehabilitation - a scoping review. Front Rehabil Sci 2021;16(2):709682. https://doi.org/10.3389/fresc.2021.709682. PMID: 36188794; PMCID: PMC9397796.
[42] Cavalcante BRR, Improta-Caria AC, de Melo VH, De Sousa RAL. Exercise-linked consequences on epilepsy. Epilepsy Behav 2021;121:108079. https://doi.org/10.1016/j.yebeh.2021.108079.
[43] Rupprecht T, Margarete P. Social aspects of epilepsy and rehabilitation. Handb Clin Neurol 2012;108:983–99.