ISRCTN89285040 https://doi.org/10.1186/ISRCTN89285040

A European study of non-progressive ataxia in children

Submission date
26/10/2025

Recruitment status
Recruiting

Registration date
28/10/2025

Overall study status
Ongoing

Last Edited
28/10/2025

Condition category
Nervous System Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Non-progressive congenital ataxia (NPCA) or ataxic cerebral palsy (CP) is a very rare early-onset condition characterized by loss of orderly muscular coordination, so that movements are performed with abnormal force, rhythm and accuracy, resulting in disturbed balance, which interferes to a variable extent with daily life. Early and appropriate management is necessary. Although scientific knowledge of this condition has progressed in recent years, we still do not know why some children present severe developmental delays and impairments. We need to study the lesions that can occur in the brain in more detail. We also need to know whether there is a genetic component to the condition. The objectives of this study are to gain a better understanding of all aspects of NPCA/ataxic CP.

Who can participate?
Children and their families with confirmed NPCA/ataxic CP will be offered inclusion in the study when they are between 5 and 8 years old.

What does the study involve?
Your child will undergo a comprehensive medical examination. This examination will take place during a consultation with one of the study's investigating physicians. The brain MRI image and the results of the genetic analysis that are already carried out or indicated in the clinical context will be sent to expert centers in Tübingen (Germany) for further analyses. As a parent, you will be asked to fill in questionnaires about your child's quality of life, your health status and the burden that your child's condition represents for you and your family. If your child has not yet undergone genetic testing, or if the project's genetic experts feel that further genetic analysis is important for your child, a blood test will be offered to your child and to you as parents (both parents).

What are the possible benefits and risk of participating?
The results will be used to establish new guidelines for diagnostic procedures, genetic work-up and care management and will enable the physicians to discuss the child's prognosis with parents.
Risks may be related to taking blood samples, and psychological consequences related to study findings.

Where is the study run from?
This study will take place in centers specialized in the care of children with NPCA in several European countries, for example Sweden, Germany, Greece, Belgium, Denmark, Norway and France.

When is the study starting and how is it expected to run for?
May 2025 to June 2027

Who is funding the study?
This study is funded by the European Joint Programme on Rare Diseases EJP RD COFUND-EJP N 825575.

Who is the main contact?
Kate Himmelmann, kate.himmelmann@vgregion.se

Contact information

Type(s)
Scientific, Principal investigator

Contact name
Dr Kate Himmelmann

ORCID ID
https://orcid.org/0000-0002-3959-9554

Contact details
Queen Silvia Children's Hospital at Sahlgrenska University Hospital
Gothenburg
Sweden
416 50
+46 (0)702 225589, +46 (0)722039472
kate.himmelmann@vgregion.se

Type(s)
Public

Contact name
Dr Catherine Arnaud

ORCID ID
https://orcid.org/0000-0002-4002-802X

Contact details
University Hospital Toulouse
Toulouse
France
31300
+33 (0)5671285
catherine.arnaud@univ-tlse3.fr

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
825575-2023-00546

Study information

Scientific Title
Non-progressive congenital ataxia advancing diagnosis to enhance chances for targeted therapy (Icke-progressiv kongenital ataxi - förbättrad diagnostik för ökad möjlighet till riktad behandling)

Acronym
ARTEMIS

Study objectives
1. To establish the detailed impairment profile of children with NPCA/ataxic CP: cognitive neuropsychiatric disorders/signs (autism, attention deficit/hyperactive disorder), speech and communications abilities, vision and hearing, gross and fine motor function, epilepsy
2. To chart developmental trajectories (based on the record of age at key developmental milestones in motor and language areas) and trace them back to infancy
3. To perform a systematic analysis of MRI brain images (available in common practice, film or digital), to carry out a detailed analysis of brain maldevelopments beyond cortical maldevelopments and of images hitherto classified in the “miscellaneous” group (see MRCI CS, Himmelmann K, Horber V et al, 2016), and to assess cerebellar and cerebral volumetry (Evans, 2006). MRI volumetry will be compared to images of typically developing age- and sex-matched children, using the NIH Pediatric Data Repository of anonymised MRI brain images.
4. To record the standardised genetic results from individuals with a firm definite genetic diagnosis
5. To perform a comprehensive advanced re-analysis of exome datasets from genetically undiagnosed cases using the diagnostic-grade open source bioinformatics pipeline megSAP (https://github.com/imgag/megSAP). New-sequencing technology will apply in unsolved cases, i. e. children still remaining without a definite diagnosis after comprehensive data re-analysis, using extended combined RNA-seq/genome sequencing (GS) approaches 'beyond the exome' and trio GS. If necessary, additional long-read (LR-)GS and complementary RNA-seq of available tissues will be performed.
6. To document the quality of life of the children (proxy report) and the family burden (psychological health of parents, perceived burden and social support, impact on work).
7. To document care use and patient journey in children with NPCA/ataxic CP.

Ethics approval required
Ethics approval required

Ethics approval(s)

approved 27/05/2025, Swedish Ethical Review Authority (Box 2110, 750 02 Uppsala, 750 02, Sweden; +46 (0)10 475 08 00; registrator@etikprovning.se), ref: 2025-03263-01

Study design
Multicenter observational cohort study

Primary study design
Observational

Study type(s)
Diagnostic, Quality of life, Other

Health condition(s) or problem(s) studied
Non-progressive congenital ataxia (NPCA), ataxic cerebral palsy

Interventions
1. Clinical assessment of ataxia
2. Impairment profile (gross and fine motor function, speech and communication function, cognitive function including neuropsychiatric disorders, epilepsy, vision and hearing)
3. Genetic analysis, and re-analysis of previous samples with new methods
4. Re-evaluation of previously done magnetic resonance imaging (MRI)

Intervention Type
Mixed

Primary outcome(s)
Characterization of non-progressive congenital ataxia (NPCA)/ataxic cerebral palsy through integral analysis of clinical features, brain imaging, and advanced genomic testing at the time of study visit

Key secondary outcome(s))
1. Clinical assessment of ataxic features includes muscle tone, tremor, balance, spasticity, and dystonia. Evaluation of ataxic features with the Scale for the Assessment and Rating of Ataxia (SARA) at the time of study visit
2. Composite multidimensional assessment of intelligence or developmental quotient (IQ or DQ), Attention-Deficit/Hyperactivity Disorder (ADHD) and/or Autism Spectrum Disorder (ASD) (according to Diagnostic and Statistical Manual of Mental Disorder V criteria) at the time of study visit
3. Speech is classified using the Viking Speech Scale (VSS) at the time of study visit
4. Communication is classified using the Communication Function Classification System (CFCS) at the time of study visit
5. Gross motor function is classified with the Gross Motor Function Classification System (GMFCS) at the time of study visit
6. Fine motor function is classified with the Bimanual Fine Motor Function (BFMF) at the time of study visit
7. Manual ability is classified with the Manual Ability Classification System (MACS) at the time of study visit
8. Epilepsy seizure onset (first year/second year/fourth year/fifth year or later) assessed by parent interview at the time of study visit
9. Epilepsy type (focal/generalized/multiple types) assessed by parent interview at the time of

study visit and retrospective data collection from medical records
10. Epilepsy frequency last year (seizure-free/seldom or monthly/weekly or daily/other (cluster or unclear) assessed by parent interview at the time of study visit and retrospective data collection from medical records
11. Epilepsy treatment: none/monotherapy/polytherapy (specify), drug resistant: yes/no, other treatment (specify), assessed by parent interview at the time of study visit and retrospective data collection from medical records
12. Visual impairment: yes/no. If yes: severe/not severe (Severe visual impairment definition: Defined as blind or no useful vision (after correction, on the better eye). If the level of vision loss is <6/60 (Snellen scale) or <0.1 (Decimal scale) in both eyes): retrospective data collection
13. Hearing impairment: yes/no. If yes: severe/not severe.(Severe hearing impairment definition: Defined as 'severe' or 'profound' hearing loss, i.e. loss greater than 70 dB (before correction, on the better ear): retrospective data collection
14. Gastrostomy/jejunostomy: Age of insertion (months) assessed by parent interview at the time of study visit and retrospective data collection from medical records
15. Neonatal imaging is classified using the Neonatal Imaging Classification System (NNICS): retrospective analysis of MRI scans through study completion, an average of 1 year
16. Postneonatal magnetic resonance imaging (MRI) is classified according to MRI Classification System (MRICS); retrospective analysis of MRI scans through study completion, an average of 1 year
17. Genomic analysis: Identification disease-associated variants. Analysis of existing or newly generated exome/genome sequencing data to identify single nucleotide variants, small insertions/deletions, structural variants, and repeat expansions. Retrospective or at the time of study participation, an average of 1 year.
18. Child's quality of life (proxy-reported) is assessed using KIDSCREEN-27. Completed by parent during study participation.
19. Parental psychological health is assessed using General Health questionnaire (GHQ-12). Completed by parents during study participation.
T. Perceived family burden is assessed using Family Impact of Childhood Disability (FICD+4), related to time, stress, finances and family relationships. Completed by parents during study participation.
20. Developmental milestones are documented through parent interview during study participation: Motor: age (months) at stable head control/sitting without support/walking alone /stands on one leg for some seconds/walks stairs without holding in, alternating language: age (months) vocalizes spontaneously/chains of syllables/mama, papa and one additional word/two-word sentences, identifies two pictures/four-word sentences. Completed at interview of parents during study participation.
21. Family interactions with healthcare system and care utilization: Age at first specialist visit, age at diagnosis therapies received, multidisciplinary evaluations, access to aids/support, social services and disability-related resources. Completed at interview of parents during study participation.

Completion date
01/06/2027

Eligibility

Key inclusion criteria
1. Male or female
2. Confirmed diagnosis of non-progressive congenital ataxia/ataxic cerebral palsy
3. Aged ≥5 and ≤8 years

Participant type(s)
Carer, Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
5 years

Upper age limit
8 years

Sex
All

Key exclusion criteria
1. Child with another diagnosis of movement disorders
2. Child with another cerebral palsy subtype

Date of first enrolment
27/11/2025

Date of final enrolment
01/06/2027

Locations

Countries of recruitment
Belgium

Denmark

France

Germany

Greece

Norway

Sweden

Study participating centre
Kate Himmelmann
Queen Silvia Children's Hospital at Sahlgrenska University Hospital

Gothenburg
Sweden
416 50

Study participating centre
Caroline Karsenty
University Hospital of Toulouse
Toulouse
France
31300 Toulouse

Study participating centre
Guro L. Andersen
Vestfold Hospital Trust
Tonsberg
Norway
3116

Study participating centre
Gija Rackauskaite
Aarhus University Hospital
Aarhus
Denmark
8200

Study participating centre
Antigone Papavasiliou
IASO Children's Hospital
Athens
Greece
15123

Study participating centre
Veronka Horber
University Hospital Tübingen
Tübingen
Germany
72076

Study participating centre
Els Ortibus
KU Leuven
Leuven
Belgium
3000

Sponsor information

Organisation
University of Gothenburg

ROR
https://ror.org/01tm6cn81

Organisation
University Hospital Toulouse

Organisation
Vestfold Hospital Trust

Organisation
Aarhus University Hospital

ROR
https://ror.org/040r8fr65

Organisation
Universitätsklinikum Tübingen

ROR
https://ror.org/00pjgxh97

Organisation
Iaso Children’s Hospital

ROR

https://ror.org/059dpw236

Organisation
KU Leuven

ROR
https://ror.org/05f950310

Funder(s)

Funder type
Government

Funder Name
European Joint Programme on Rare Diseases (EJP RD) COFUND-EJP No 825575

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study är unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 1.0		28/10/2025	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes