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Research into clinical and MRI measures to get understanding of the neuropsychological outcome of children undergoing surgery for a brain tumor

Submission date
20/12/2023

Recruitment status
Recruiting

Registration date
28/05/2024

Overall study status
Ongoing

Last Edited
28/05/2024

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
Central nervous system (CNS) tumours comprise 25% of all childhood cancers, and more than half of these are located in the cerebellum. After an operation for such a tumour, up to 25% of children may experience cerebellar mutism syndrome (CMS). It is characterized by mutism, hypotonia, ataxia and irritability, and the exact causes have yet to be identified. Although a cure may have been achieved for their brain tumour, the CMS and its consequences can still pose a lifelong challenge for these children. Since about half of paediatric brain tumours are located in the posterior fossa and require surgery, CMS is a common and serious issue in paediatric neuro-oncology. The main aim of this study is to investigate early clinical and neuroradiological (MRI) predictors of neuropsychological outcomes in children with posterior fossa tumors. Additionally, the study aims to identify group differences and changes over time in neuroradiological and neuropsychological measures for children with higher versus lower CMS symptom severity.

Who can participate?
Children participating in the European CMS study are also eligible for the FASTigial study. Children (2-18 years old) requiring surgery for a cerebellar (posterior fossa) tumor at one of the participating centers will be included after informed consent has been obtained. Additionally, patients must understand and be able to speak the local language. In contrast to the European CMS study, patients who have undergone surgery previously CANNOT participate in FASTigial.

The targeted number of included patients is 210, with 80 children expected to be included at the Princess Maxima Center for Pediatric Oncology.

What does the study involve?
Patients participating in the study will be treated according to local standards. Additionally, we will perform neuropsychological tests before surgery, directly after surgery, and 12 months after surgery using digital tests lasting about 30 minutes each time. While the child completes the neuropsychological tests, the parent(s) will be asked to complete several questionnaires.

Furthermore, the child will undergo an MRI scan as part of standard care. Two additional MRI sequences will be added to the clinical protocol, including diffusion and perfusion scan techniques.

What are the possible benefits and risks of participating?
Participation in the study will not impact or interfere with the child's treatment plan. The child will not experience any extra benefits or risks. The administration of neuropsychological tests carries no risk. The additional MRI sequences are obtained when the patient undergoes a clinical MRI, thus the patient is not at risk.

Patients may even benefit from additional explanations and guidance provided by the researchers. In contrast, the study yields crucial insights into the etiology of cerebellar mutism and the factors influencing its onset and recovery.

Where is the study run from?
The Princess Máxima Center Utrecht (the Netherlands)

When is the study starting and how long is it expected to run for?
From April 2024 to October 2027

Who is funding the study?
Children Cancer Free Foundation (Stichting Kinderen Kankervrij) (the Netherlands)

Who is the main contact?
Marita Partanen, M.H.Partanen@prinsesmaximacentrum.nl

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Protocol serial number
MN21FAS

Study information

Scientific Title
FASTigial: Finding Anatomical SubsTrates of neuropsychological outcome in children with posterior fossa tumors (add-on project on the European CMS study)

Acronym
FASTigial

Study objectives
It is expected that clinical criteria, CMS symptom severity, and changes in neuroradiological findings over time will predict neuropsychological outcome at 12 months after surgery. Patients with higher versus lower CMS symptom severity will have greater pre- and post-operative damage to white matter tracts (DTI), leading to changes in perfusion (ASL). Also, those with higher versus lower CMS severity will have significant impairments across neuropsychological domains, particularly in executive functioning, attention, processing speed and emotional-behavioral domains. Some deficits will be shown at the pre-surgery phase, but impairments will become more apparent post-surgery. Some children will show recovery over time, however, those with greater CMS symptoms will have slower recovery.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 03/04/2024, Medisch-Ethische Toetsingscommissie NedMec (Huispost D01.343 Postbus 85500, Utrecht, 3508 GA, Netherlands; +31 88-7556376; metc@nedmec.nl), ref: NL85971.041.23

Study design
Multicenter observational study

Primary study design
Observational

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

Health condition(s) or problem(s) studied
Newly diagnosed pediatric brain tumors located in the posterior fossa

Interventions
For this multicenter observational study, patients participating in the study will be treated according to local standards. Additionally, we will conduct neuropsychological tests preoperatively, postoperatively, and 12 months after surgery using digital tests that take approximately 30 minutes each time. While the child completes the neuropsychological tests, the parent(s) will be asked to complete several questionnaires. Furthermore, the child will undergo MRI scans as part of standard care. Two additional MRI sequences will be added to the clinical protocol, including diffusion (DTI) and perfusion (ASL) scan techniques. A neurological

scale will be completed. Other medical information will be retrieved from the database of the European CMS study (to which the FASTigial study is an add-on)(www.ClinicalTrials.gov; NCT02300766).

Intervention Type
Other

Primary outcome(s)
1. Age-standardized performance on executive functioning (neuropsychological domain) measured using questionnaires filled in by parents preoperatively, postoperatively, and 12 months after surgery.
2. White matter integrity and perfusion in the brain measured using MRI and clinical data (e.g., age, treatment) will be used to investigate early clinical and neuroradiological predictors of neuropsychological outcome preoperatively, postoperatively, and 12 months after surgery.

Key secondary outcome(s))
1. Age-standardized performance on neuropsychological measures, measured using computerized tests (Cogstate) and questionnaires preoperatively, postoperatively, and 12 months after surgery.
2. Clinical, neuroradiological (white matter integrity and perfusion) and neuropsychological variables will be collected to identify group differences and changes over time in posterior fossa tumor patients who have higher versus lower CMS symptom severity preoperatively, postoperatively, and 12 months after surgery.

Completion date
01/10/2027

Eligibility

Key inclusion criteria
Eligible for European CMS study
1. Age 2-18 years at the date of first imaging showing this tumour
2. Understanding and speaking of local language by patient and/or parents

Inclusion criteria European CMS study:
1. Age <18 years at the date of first imaging showing this tumour
2. Tumour in the cerebellum/4th ventricle/brainstem with the intention to treat with surgical resection or open biopsy.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
2 years

Upper age limit
18 years

Sex
All

Key exclusion criteria
1. Patients who have had previous surgery on the posterior fossa
2. No informed consent from custodial parent(s) and/or patient

Date of first enrolment
01/04/2024

Date of final enrolment
01/10/2026

Locations

Countries of recruitment
Netherlands

Study participating centre
Princess Maxima Center for Pediatric Oncology
Heidelberglaan 25
Utrecht
Netherlands
3584 CS

Sponsor information

Organisation
Princess Máxima Center

ROR
https://ror.org/02aj7yc53

Funder(s)

Funder type
Not defined

Funder Name

Stichting Kinderen Kankervrij

Alternative Name(s)
Children Cancer Free Foundation, Foundation KiKa, Kika8118, Kiki_KinderenKankervrij, Stichting Kinderen Kankervrij (KiKa), KiKa

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Netherlands

Results and Publications

Individual participant data (IPD) sharing plan
During the conduct of the study the data is under embargo. After study completion data sharing plans will be made available.

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