# Research on the mechanism of cognitive decline in patients after cerebellar pontine angle tumour surgery

Published: 07-02-2024 Last updated: 25-09-2024

Our aim is to identify cognitive dysfunction in patients with a cerebellar pontine angle tumour (koos classification grade 4 schwannoma) that have been operated in order to prevent cognitive decline in future patients. For this purpose, we want to...

Ethical review Approved WMO

**Status** Pending

Health condition type Nervous system neoplasms benign

**Study type** Observational non invasive

# **Summary**

#### ID

NL-OMON56566

#### Source

**ToetsingOnline** 

#### **Brief title**

Cognitive impairments after CPA surgery

#### **Condition**

- Nervous system neoplasms benign
- Nervous system, skull and spine therapeutic procedures

#### **Synonym**

cerebellar pontine angle tumour, vestibular schwannoma

#### Research involving

Human

## **Sponsors and support**

**Primary sponsor:** Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W, subsidie aangevraagd

1 - Research on the mechanism of cognitive decline in patients after cerebellar pont ... 14-06-2025

bij radboud oncologiefonds

#### Intervention

**Keyword:** Cerebellopontine angle surgery, Cognition, Tractography, Vestibular schwannoma

## **Outcome measures**

#### **Primary outcome**

The main study parameters of this study are:

- patient variables (age, sex, level of education, unilateral hearing loss, tinnitus).
- tumour parameters (diameter, volume, side, etc).
- surgical parameters (length of operation, blood loss, etc).
- neuropsychological testing and/or its different domains
- CCAS/Schmahmann scale.
- MR Imaging findings (degree of oedema, anatomical displacement, etc).
- DWI findings (fractional anisotropy (FA), axial diffusivity (AD), radial diffusivity (RD), etc).

The primary outcome measures are:

- scores on the different domains of extensive neuropsychological testing
- scores on CCAS/Schmahmann scale
- abnormalities on tractography

#### **Secondary outcome**

The secondary outcome measures are:

- additional MR Imaging findings in correlation to neuropsychological testing.

2 - Research on the mechanism of cognitive decline in patients after cerebellar pont ... 14-06-2025

# **Study description**

#### **Background summary**

Vestibular schwannoma (VS) is a benign and rare tumour localized in the cerebellopontine angle (CPA), accounting for 5-10% of all intracranial tumours (1). In the Netherlands, around 600 patients each year are diagnosed with a tumour in the cerebellopontine angle region, of whom 250 patients end up at Radboud University Medical Center (UMC)(2,3,4). Most often surgery is not indicated and other treatment options like watchful waiting and radiosurgery is sufficient.

However in larger tumours, often accompanied by severe clinical symptoms due to their location close to vital anatomical structures, i.e., the cranial nerves and/or the brainstem, surgery is the first choice of treatment (Koos classification grade 4)(5). In Radboud UMC, this surgery is done on 15-20 patients per year. Symptoms include, amongst others, impaired facial nerve function, progressive unilateral hearing loss, tinnitus and vertigo (6).

Resection of a CPA tumour involves major risks. For example, approximately 10-25% of patients report cognitive complaints postoperatively, which they consider very disabling to their quality of life and may lead to lifelong residual symptoms. Since this is not routinely included in the follow up, this percentage is only a rough estimate.

To date, there are few reports on whether a CPA tumour itself can cause cognitive dysfunction, and the number of reported cases is small. Goebel et al. (2018) included 45 patients with an untreated CPA tumour and found that 69% reported neurocognitive problems (7). To date, there are no studies available concerning cognitive dysfunction after CPA surgery.

More importantly, little is known about the underlying mechanism. Deng et al. (2022) demonstrated that cognitive decline in patients with an untreated VS was correlated to changes in white matter pathways relative to healthy control patients. The authors found that in patients with VS decline of general cognitive function, attention, memory, executive control, and visuospatial and visuoperceptual abilities was related to white matte damage in the minor forceps of the corpus callosum compared to control patients (8).

To our knowledge, no previous studies interested in cognitive decline and white matter fiber tracts after CPA surgery are available. At present, there are few studies on the white matter fiber tracts of cerebellar systems in paediatric tumours. Emotional, cognitive, and behavioural disturbances have been described in children after surgery for tumours in the posterior cranial fossa using various overlapping terms like cerebellar mutism syndrome (CMS), posterior

fossa syndrome (PFS) and cerebellar cognitive affective syndrome (CCAS) (9, 10). Recent investigations have led to new insights that damage to the cerebellar peduncles, seen in tractography correlates with decline in cognitive function. The current hypothesis is that CCAS arises from damage to the tractus cerebello-dento-thalamo-corticalis which causes interruption of important circuits and leads to hypofunction of supratentorial cortical areas (9, 10). In our opinion, there could possibly be a similar explanation for cognitive dysfunction after CPA surgery.

#### Study objective

Our aim is to identify cognitive dysfunction in patients with a cerebellar pontine angle tumour (koos classification grade 4 schwannoma) that have been operated in order to prevent cognitive decline in future patients. For this purpose, we want to subject a group of patients who underwent resection of a CPA tumour and the control group (diagnosed with a Koos classification grade 1-4, however without indication for surgery) to extensive neuropsychological testing in combination with a comprehensive MRI scan to answer the following primary questions:

- 1. How common is cognitive dysfunction (as detectable by neuropsychological testing and the CCAS/Schmahmann scale) in patients after CPA surgery compared to control patients?
- 2. Is there a correlation between cognitive dysfunction of patients after resection of a CPA tumour (Koos classification grade 4) and abnormalities on the MRI scan (both anatomical (T1/T2/Flair) and tractographic (DWI; fractional anisotropy or ADC)) compared to control patients?

#### Study design

This is the first study concerning patients with cognitive dysfunction after CPA tumour surgery. Due to the low annual incidence of VS, this explorative study has a cross sectional study design.

#### Study burden and risks

The nature and extent of the burden and risks associated with participation in this study are low and will have no therapeutic consequences for participants. As mentioned before, this study consists of a comprehensive neuropsychological examination and the CCAS/Schmahmann scale, both in which various cognitive domains are measured including attention and concentration, executive functions, memory, language, visual-spatial skills, abstraction ability and neuropsychiatric symptoms. The test takes about 1-1.5h and a visit to the Radboud UMC in Nijmegen is necessary.

In addition, participation includes a comprehensive MRI without contrast with a duration of up to 1h at the Donders institute. If there is a contra-indication for MRI, the patient is not eligible for the study and will be excluded. The burden and risks of MRI are estimated to be low.

## **Contacts**

#### **Public**

Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 10 Nijmegen 6525 GA NL

#### **Scientific**

Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 10 Nijmegen 6525 GA NL

## **Trial sites**

#### **Listed location countries**

**Netherlands** 

# **Eligibility criteria**

#### Age

Adults (18-64 years) Elderly (65 years and older)

#### Inclusion criteria

- Patients diagnosed with a cerebellar pontine angle tumour (Koos classification grade 4 schwannoma) that have been operated in the past.
- Control population consisting of patients with unilateral hearing loss due to a cerebellar pontine angle tumour Koos classification grade 1-4. These control patients have a \*wait and see\* policy with annual follow up and did not have surgery in the past. Control patients will be matched (as far as possible) to
  - 5 Research on the mechanism of cognitive decline in patients after cerebellar pont ... 14-06-2025

the study population on Koos grade, age, level of education, hearing loss and tumour side.

- > = 18 years of age
- Dutch proficiency

#### **Exclusion criteria**

- contra-indication for MR imaging
- history of neurofibromatosis type II
- history of cerebellopontine angle surgery or Gamma Knife radiation
- secondary hydrocephalus due to surgery
- concurrent neurological or psychiatric illness
- not able to give informed consent

# Study design

## **Design**

Study type: Observational non invasive

Intervention model: Other

Allocation: Non-randomized controlled trial

Masking: Open (masking not used)

**Primary purpose:** Prevention

#### Recruitment

NL

Recruitment status: Pending

Start date (anticipated): 01-02-2024

Enrollment: 60

Type: Anticipated

# **Ethics review**

Approved WMO

Date: 07-02-2024

Application type: First submission

Review commission: CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date: 04-09-2024

Application type: Amendment

Review commission: CMO regio Arnhem-Nijmegen (Nijmegen)

# **Study registrations**

# Followed up by the following (possibly more current) registration

No registrations found.

# Other (possibly less up-to-date) registrations in this register

No registrations found.

# In other registers

Register ID

CCMO NL84932.091.23