Identification of premotor white matter tracts involved in language before and after resection of tumors in the left hemisphere.

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Our hypothesis is that a left hemisphere tumor causes language dysfunction by mass effect on or infiltration of white matter tracts connecting Wernicke's area with Broca's area and between Broca's area and the SMA. The neurosurgical...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Nervous system neoplasms malignant and unspecified NEC
Study type	Observational invasive

Summary

ID

NL-OMON38935

Source
ToetsingOnline

Brief title
Language tracts before and after resection of tumors.

Condition

- Nervous system neoplasms malignant and unspecified NEC

Synonym
brain neoplasma, brain tumor

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Intervention

Keyword: Diffusion tensor imaging, Language, Tumor

Outcome measures

Primary outcome

(1) Evaluation of the white matter tracts between Broca's area and the ventral premotor cortex with the SMA and Wernicke's area in the left hemisphere to assess if they can be identified. The mirrored equivalent in the right hemisphere functions as a reference. (2) To assess if there is a correlation between language dysfunction and tumor involvement of these connections. (3) Comparison of the volume of connections in the pre- and postoperative situation. (4) To assess if there is a relation between disruption of the specific SMA connections and motor dysfunction (especially bilateral tasks).

Language dysfunction will be quantified with the Boston naming test, fluency tests (letter, semantic, verbs, spontaneous speech), the Token test (from the Aachen Aphasia test), object naming and action naming. Language tests will be correlated with the amount of white matter tracts between the areas of interest.

Secondary outcome

The amount of resection of tumors. Neurological deficit. This is descriptive.

Study description

Background summary

The mouth and hand are two important effector systems (speaking, writing) to express yourself in language. Input to the involved motor cortex is channeled via premotor cortex areas. Dysfunction in language is classically caused by disturbances in the left inferior frontal gyrus (Broca's area, expressive aphasia) or the left posterior temporal area (Wernicke's area, receptive aphasia). Conduction-aphasias are caused by damage to the arcuate fascicle, the white matter tract connecting the two language areas. In practice however, aphasias are a heterogenous group, with both Broca- and Wernicke-like symptoms. Dysfunction of language can also be caused by damage to the supplementary motor area (SMA), which varies from less spontaneous speech to mutism. Both for tumors in the SMA and perisylvian tumors it is difficult to predict postoperative deficit preoperatively. It is important to realize that a function is not isolated in a specific cortical area, but is represented by a broader network of interconnected cortical areas. Aside from disturbance of these connections caused by the tumor, the neurosurgical approach to the tumor may also be a cause of disturbing these connections. The effects of a tumor on language-related connections to the premotor cortex are evaluated in this study using DTI.

The SMA is located in the dorsomedial frontal cortex, anterior of the representation of the legs in M1, and can be regarded as the medial extension of the premotor cortex. The SMA is somatotopically organised. Orofacial movements are evoked with anterior stimulation of the SMA, whereas more posterior stimulation evokes arm and leg movements. A substantial part of the cells in the piramidal tract originates directly from the SMA. Apart from direct output to the piramidal tract, the SMA is also a secondary motor area. Activation of the SMA is associated with starting movements, the performance of more complex movements such as bilateral movements or the selection of movements and motor learning. There are strong interhemispheral connections between the two SMAs. Neuronal activity in the SMA is associated with both contra- and ipsilateral movements. The SMA is connected with the piramidal tract, primary motor cortex, other premotor areas and primary and secondary sensory areas.

A lesion in the SMA leads to dysfunction in the performance of bimanual movements in monkeys. In humans, surgical excision of the SMA can lead tot typical postoperative deficit, called the SMA syndrome, with many different symptoms. Most of the time there is contralateral motor dysfunction, varying from a complete hemiparesis to less spontaneous motor output, also called motor neglect. The motor deficit is unpredictable, but seems to be more prevalent when the resection includes more dorsal parts of the SMA, close to the motor strip. Language dysfunction can also be part of the SMA syndrome (less spontaneous speech, mutism). The broad clinical picture may suggest a heterogenous group. However, the resemblance is that all postoperative deficits

recover almost completely within weeks to months. With fMRI is has become clear that postoperative deficit is associated with a stronger activation of premotor areas (SMA and laterale premotor cortex) in the healthy hemisphere. Furthermore, there was more activation in the premotor cortex of the healthy hemisphere, which was related to the extent of resection of preoperative SMA activation. This suggests that there is plasticity.

Study objective

Our hypothesis is that a left hemisphere tumor causes language dysfunction by mass effect on or infiltration of white matter tracts connecting Wernicke's area with Broca's area and between Broca's area and the SMA. The neurosurgical operation can have influence on these connections (by a decrease in mass effect or by resection of infiltrated areas during which also functional white matter tracts are resected). Functional recovery postoperatively can be caused by recovery of existing connection and/or functional reorganization, where other connections take over the affected functions. Language dysfunction will be related to the disturbance of white matter tracts to gain more insight in the nature of aphasias. The involved white matter tracts will be quantified using diffusion tensor imaging (DTI). Also, the relation between disturbance of SMA connections and motor dysfunction (especially bilateral tasks) is examined.

Study design

DTI images in 60 directions will be made in subjects with a intraparenchymal tumor in the left hemisphere. During a period of two years patients will be included in this observational study.
Standard neurological examination will be performed preoperatively to document preoperative dysfunction. This is a baseline for later examinations. Phase and antiphase movements will be tested as a specific parameter for SMA function. Language functions and more general neuropsychological examinations will be quantified by the participating neuropsychologist with standard tests. Also, handedness is assessed preoperatively with the Edinburgh Handedness Inventory. The neurological examination en testing of language functions will be repeated postoperatively and at discharge to document possible deficit. These pre- and postoperative neuropsychological and neurological tests are part of the standard work-up in this patient population. Within 48 hours after operation a MRI with diffusion-weighted imaging (DWI) will be made to assess the postoperative picture. This is also part of the standard care in these patients. After a mean of 4,5 months another DTI scan will be made to compare the white matter tracts with the preoperative situation. At that time the standard postoperative neurological and neuropsychological examination will be repeated. General patient characteristics such as date of birth, gender, time to recovery of deficit and pathology of the tumor will be documented.

First the ventral premotor cortex, SMA and language areas of Broca and Wernicke

will be identified as a base for seed-based tractography to identify white matter tracts and displacement by tumor. Using seed-based tractography we track the healthy contralateral hemisphere to see if there are stronger connections in the homologous equivalents of the mentioned areas. The areas of Broca and Wernicke in the right hemisphere will be defined on the same coordinates as the left hemisphere where we mirror left and right. At first we investigate if there is a relation between the disruption of white matter tracts and preoperative symptoms or postoperative deficit. We compare preoperative and late postoperative DTI images to assess if there is irreversible damage or that there is a decreased functional resolution caused by edema. A difference in white matter tracts is characterized with probabilistic tractography in FMRIB Software Library (FSL).

Study burden and risks

Extra investigations in these subjects:
• A preoperative DTI investigation in the Neuro-Imaging Center.
• Within a mean of 4,5 months postoperatively an extra DTI investigation should take place in the Neuro-Imaging Center.

The use of MRI is considered very safe, especially when there is good attention for contra-indications. The risk is negligible and the burden is small so we think this research is justifiable.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Right-handed adult patients 18 years and older with a intraparenchymal brain tumor in the left hemisphere without other neurological or psychiatric disorders.

Exclusion criteria

Patients with more than one tumor. Patients who suffer from other specific neurological or psychiatric disorders than caused by the tumor will be excluded. Patients who cannot go in the MRI scanner are also excluded.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-12-2013
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO
Date: 10-09-2013

Application type: First submission

Review commission: METC Universitair Medisch Centrum Groningen (Groningen)

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	NL45023.042.13