Childhood Brain Tumours: Epidemiology and Risk factors

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WHO workshop
Sensitivity of Children to EMF exposures
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• Descriptive epidemiology of childhood Central Nervous System (CNS) tumours

• Identify differences between cancers and CNS tumours in adults and children

• Risk factors

• Considerations for studying children and mobile phone use

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Childhood CNS tumours: basic facts 1

- Second most common childhood malignancy approximately 20% of all childhood cancers
- Most common solid tumour
- Incidence rate 3.9 per 100,000 pyrs in 0-19 yr olds (CBTRUS 2003/4, includes both malignant and benign)
- New cases/yr in US 2,330 under 15 years
Childhood CNS tumours: Basic facts 2

- Male excess: M:F ratio 1.2:1

- Ethnic origin: white populations may be at higher risk than non-white

- Geography: incidence in Africa 11 /million, Japan, US, Europe 20-30 /million

- Social class: higher risk possibly associated with higher social class
### Classification of childhood CNS tumours

*International Classification of Childhood Cancers (ICCC) Kramarova IARC no 29. 1996*

#### Group III CNS and miscellaneous intracranial neoplasms

<table>
<thead>
<tr>
<th>Distinct histological subtypes</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>a Ependymomas</td>
<td>10</td>
</tr>
<tr>
<td>b Astrocytomas</td>
<td>40-50</td>
</tr>
<tr>
<td>c Primitive Neuroectodermal Tumours (PNET) (medulloblastomas)</td>
<td>25</td>
</tr>
<tr>
<td>d Other gliomas</td>
<td>10</td>
</tr>
<tr>
<td>ef Other specified and unspecified CNS</td>
<td>8-13</td>
</tr>
</tbody>
</table>
Age specific incidence rates for CNS tumours (0-29 years) in Yorkshire 1990-2001

All CNS tumours

Astrocytomas

Medulloblastomas/PNET

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Incidence rates (per million pyrs) for CNS tumours (0-29 years) 1990-2001 in Yorkshire

Incidence rates for CNS tumours (0-29 years) 1990-2001 in Yorkshire

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Time trends in childhood CNS tumours

• Is the incidence rising??

• Evidence suggests approximate 2-3% rise from 1970s

• Increases vary by age, sex, tumour type and ethnic group

• Debate continues over whether increases result from improved detection and registration
Cancers in adults and children: differences

1. Occur in tissues with different foetal origins

Adults: carcinomas which develop in epithelial or ‘covering’ tissues
Children: embryonal origin – mesodermal (non-epithelial) tissues

2. Different disease classification scheme

Adults: classified by topography i.e. anatomical site not histological subtype e.g. lung
Children: classified by morphology i.e. histological picture e.g. germ cell tumour
CNS tumours show differences between adults and children

1. Different tumour types predominate

   Adults: fewer Primitive Neuroectodermal Tumours (PNET) (medulloblastoma)
   Children: fewer meningiomas (tumours of brain ‘covering’, the meninges)

2. Astrocytomas/gliomas different histologies

   Adults: gliomas (44% of all CNS tumours)
   Children: juvenile pilocytic astrocytomas (19%)

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CNS tumours show differences between adults and children

3. Proportion of all cancers
   - Adults: less than 2% of all cancers
   - Children: 20% of all cancers under 15 years

4. Vary by anatomical site
   - Adults: more above tentorium
   - Children: more commonly below tentorium
Risk factors for childhood CNS tumours

Causes largely unknown

Genetic predisposition

Environmental influences
Genetic predisposition

Genetic syndromes  e.g. neurofibromatosis

Familial cancers  inconsistent evidence (parent/sib)

Second primary tumours  little evidence following untreated tumours
Genetic predisposition

Predisposing genes: NF1, NF2, TP53

Polymorphisms: oxidation, detoxification, DNA repair, immune functioning yet to be studied in large samples

Estimates: 5% childhood CNS tumours

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Environmental risk factors: considerations

**Time window of exposure**
- Preconception – mothers/fathers
- In-utero – mothers
- Postnatal – child (mothers/fathers)

**Type of study**
- Biases
- Confounding

**Exposure estimates**
- Measured
- Reported

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Environmental risk factors

- Ionising radiation
- Chemicals
- Immune factors
- ELF - EMF
## Ionising radiation

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
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<tbody>
<tr>
<td>Preconception</td>
<td>No consistent association apparent but studies limited which identify CNS tumours</td>
</tr>
<tr>
<td>In-utero</td>
<td>For abdominal X-rays early studies in 1970s showed raised risks but no associations more recently</td>
</tr>
<tr>
<td>Postnatal</td>
<td>Increased risk with high therapeutic doses e.g. following radiotherapy for a first cancer, tinea capitis treatment</td>
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<td>Little evidence for other X-ray exposures Inconsistent evidence for dental X-rays</td>
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Chemicals: 1

- N-nitroso compounds are mutagenic and transplacental neurocarcinogens in animal models.
- Human exposure from diet, drugs, beer, smoking…..
- Raised risk for maternal cured meat consumption during pregnancy consistent association
- Protective effect of vitamin consumption during pregnancy
Chemicals: 2

- No associations with maternal smoking
- N nitroso hypothesis not consistently supported
- Extensive list of other associations observed but results are inconsistent
  
e.g. some paternal occupations
  residential pesticides

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Immune factors: 1

- Viruses induce brain tumours in animal models; little support for this occurring in humans.

- Atopic diseases, markers of immune dysfunction are ‘protective’ for adult gliomas; not been investigated in children.
Immune factors: 2

- Clustering, seasonality of diagnosis, population mixing indicate an infectious aetiology (UK studies)

- Further investigations may be fruitful
ELF EMF (30-300Hz, 50/60 Hz)

NRPB 2004

…..overall evidence for adverse effects of EMFs on health at levels of exposure experienced by the general public is weak. The least weak evidence is for the exposure of children to power frequency magnetic fields and childhood leukaemia.

• Residential exposure
• Excess risk above 0.4μT/ 0.3μT (pooled analyses)
ELF EMF (50/60 Hz)

- Childhood CNS tumours: fewer studies
- Generally combine all subtypes
- Early studies in the Nordic countries and USA found some positive associations
- More recent investigations have not confirmed earlier findings
ELF EMF (50/60 Hz)

Recent studies showing no associations

UK Children’s Cancer Study (1999)  
- household measurements  
- CNS cases n=387

UK Children’s Cancer Study (2000)  
- proximity to power lines  
- CNS cases n=614

German study (Schuz et al 2001)  
- household measurements  
- CNS cases n=62

Overall size/power lower than leukaemia BUT  
Numbers of cases highly exposed (≥0.4μT) similar

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ELF EMF (30-300Hz, 50/60 Hz)

NRPB 2004

.....overall EVIDENCE for excess cancer risks (including CNS tumours) in children and adults as a result of exposure to ELF EMF is INADEQUATE

Extension of evidence base required

?pooled analysis
Mobile phone use and child health

Currently no published studies on children

Adult studies

• On balance mobile phone use currently does not indicate increased risk for CNS tumours

• Acoustic neuromas, rare benign tumour of acoustic nerve. No evidence from ‘small studies’ of any increased risk
Mobile phone use and child CNS tumours

Considerations for the future: 1

• Clear definition of disease: Biological diversity

• Age of exposure: latency for tumour development unclear

• Could exposure in childhood increase risks in later life?

• Rarely occur in the population: study size an issue

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Mobile phone use and child CNS tumours

Considerations for the future: 2

*Time period of exposure*: preconception, in-utero, POSTNATAL

*Type of study*: case control, cohort studies, population studies

• Case control retrospective studies of children extended to young adults to capture any effect
• Biases in control group
• Unmeasured confounding
Mobile phone use and child CNS tumours

Considerations for the future: 3

*Cohort studies*: very large base populations required could look at other health outcomes

*Incidence studies*: correlate patterns of use in children with changing patterns of CNS cancers, e.g., CNS tumours or acoustic neuromas appearing at younger ages

- Timescale extensive
- Registration of CNS tumours not universally of high quality or timely

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Mobile phone use and child CNS tumours

Considerations for the future: 4

Exposure estimates: informed by current studies e.g INTERPHONE study

INTERPHONE Study
• Large international case control study (13 countries)
• Focussing on relating reported phone use to good exposure estimates
• Power output related to frequency of use, make and model of phone, location of use (urban/rural)
Future studies will need to be carefully planned!