Space-time clustering analyses of childhood cancers supports a common infectious aetiology

Richard J.Q. McNally (1), Osborn B. Eden (2), Freda E. Alexander (3), Anna M. Kelsey (4) and Jillian M. Birch (1)

(1) Cancer Research UK Paediatric and Familial Cancer Research Group, Central Manchester and Manchester Children’s University Hospitals NHS Trust, Manchester M27 4HA, UK.

(2) Academic Unit of Paediatric Oncology, Central Manchester and Manchester Children’s University Hospitals NHS Trust and Christie Hospital Trust, Wilmslow Road, Manchester M20 4BX, UK.

(3) Department of Public Health Sciences, The University of Edinburgh Medical School, Teviot Place, Edinburgh EH8 9AG, UK.

(4) Department of Histopathology, Central Manchester and Manchester Children’s University Hospitals NHS Trust, Manchester M27 4HA, UK.

Correspondence: Dr Richard J.Q. McNally, Cancer Research UK Paediatric and Familial Cancer Research Group, Stancliffe, Royal Manchester Children’s Hospital, Hospital Road, Manchester M27 4HA, UK.
Tel: +44 (0) 161 7272522; Fax: +44 161 7272508; E-mail: richard.mcnally@man.ac.uk.

Summary.

We have identified cross-space-time clustering between cases of childhood cancer from specific diagnostic groups. These findings suggest a common infectious aetiology for these specific types of childhood cancer.

Introduction.

In previous studies (Birch et al, 2000; McNally et al, 2002a, 2002b, 2003, 2004) we demonstrated significant space-time clustering amongst cases of ALL, astrocytoma, soft tissue sarcoma and Wilms’ tumour. We hypothesised that there may be a common aetiology particularly between some of these diagnostic groups. The aim of the present study was to test this hypothesis by analysing for cross-clustering between cases in different diagnostic groups.

Materials and Methods.

Cases included in the Manchester Children’s Tumour Registry during the period 1954-2001 were analysed. Knox tests for space-time interactions between cases were applied with fixed thresholds of close in space, <5km and close in time, <1 year apart, to determine whether there are more pairs occurring in close proximity than expected by chance (Knox, 1964). Tests were repeated replacing geographical distance with distance to the Nth nearest neighbour [NN] to adjust for population density. N was chosen such that the mean distance was 5km. Data were also examined by a second order procedure based on K-functions to allow for multiple testing and boundary effects (Diggle et al, 1995). Reference points in time and space were dates and addresses at birth and diagnosis respectively.
Results.

All four methods showed statistically significant (p<0.05) cross-space-time clustering between cases of HD and astrocytoma, ALL and astrocytoma, and ALL and NHL, based on time and place of birth; between cases of NHL and PNET’s, and AML and peripheral neuroectodermal tumours, based on time and place of diagnosis; between cases of ALL and PNET’s, and ALL and peripheral neuroectodermal tumours, based on time of diagnosis and place of birth; between cases of ALL and peripheral neuroectodermal tumours based on time of birth and place of diagnosis. There was little evidence of cross-clustering between Wilms’ tumours, soft tissue sarcomas and other malignancies respectively.

Conclusions.

These findings are consistent with a common infectious aetiology for certain haematological and neural malignancies in children.

Acknowledgement.

The Manchester Children’s Tumour Registry is supported by Cancer Research UK. Jillian M. Birch is Cancer Research UK Professorial Fellow in Paediatric Oncology and Osborn B. Eden is Cancer Research UK Professor of Paediatric Oncology at the University of Manchester. We thank Mr. D.P. Cairns, Mrs. E.A. Dale, Mrs. D.A. Elliott, Mrs. J.F. Hogg and Mr. C. Nikolaisen for all their hard work on data processing and verification.

References.


