ARTICLE

The ‘late effects’ of paediatric brain tumours

Helen Stocks, Kate Ablett and Matthew Morrall on the contribution of neuropsychological assessment to paediatric oncology services

This article explores the cognitive and learning difficulties experienced by children diagnosed with brain tumours and the subsequent impact on various areas of their life. It also examines current treatment practice for brain tumours and dilemmas faced by the treating multi-disciplinary team.

A three-year-old girl presents at a regional A&E experiencing visual disturbance, difficulties with movement and nausea. Neuroimaging identifies a space-occupying lesion in her brain, and the regional paediatric neurooncology service is informed. Further detailed neuroimaging and a biopsy identify a malignant ‘standard risk’ medulloblastoma brain tumour. The child's parents are informed of the outcome and are told that following the planned neurosurgical removal of the tumour, treatments will include six weeks of daily cranio-spinal radiotherapy as well as approximately 12 months of chemotherapy. The child and parents are informed that the treatments may produce unwanted side-effects and, in particular, late effects. A member of the treating team explains to the parents that their child may experience longstanding cognitive and learning impairments which may have an impact on various aspects of the child’s school, home and social life.

This devastating scenario contains typical clinical features and raises important questions. What exactly do cognitive late effects entail and how should they be assessed and managed? What effects will surviving a brain tumour have on the child’s overall quality of life? How can clinical psychology services, particularly neuropsychological evaluation, contribute to the care of the child and multidisciplinary practice?

A medulloblastoma, as mentioned in the clinical scenario, is one of the range of brain tumours of the central nervous system (CNS). CNS tumours are the second most common form of paediatric cancer, accounting for 21 per cent of cancers in males and 23 per cent of cancers in females diagnosed in the 0–14 years age group in the UK (ONS, 2008). Paediatric cancers have seen significant improvements in treatment outcomes over the past few decades, with survival rates for children diagnosed with CNS cancers increasing (ONS, 2008). The significant improvement in survival rates is due to treatment advances and increased participation in clinical trials (Grundy & Walker, 2010). Increased participation in research has been important as this allows for a better understanding of the biological features of particular tumours, which, in turn, has meant that more tailored treatments can be developed for each type of brain tumour. For medulloblastomas, there have been recent advances in identifying their biological markers, which may better predict patient outcomes (Pizer & Clifford, 2009) and lead to selecting treatments with improved survival rates.

As survival rates have increased and more children are surviving for longer, ‘late effects’ have become increasingly apparent to patients and the clinical community. Cognitive late effects are essentially emerging problems of thinking and learning, and it has been found that these may worsen over time and can be caused both by the tumour and by the treatments used (Grill et al., 2004). In terms of treatments, radiotherapy may lead to poorer learning outcomes and these cognitive trajectories may plateau over time (Askins & Moore, 2008; Fouladi et al., 2005). Furthermore, the most severe cognitive outcomes are associated with being younger at the time of radiotherapy treatment (Kulkarni et al., 2004). In the UK it is now recommended that radiotherapy for brain tumours is delayed or avoided in children who are less than 36 months of age due to the vulnerable immaturity of the brain and its developing cognitive processes (Grundy et al., 2007).

The potential effects of radiation on
cognition and subsequent learning pose a substantial dilemma for the treating team. An increase in the chances of patient survival has to be weighed up against the possible occurrence of negative neurocognitive sequelae (Grundy & Walker, 2010). Processes such as attention and memory may be affected severely. Problems with these aspects of cognition may result in problems with learning, which in turn affect academic attainment and eventual employability: approximately 70 per cent of brain tumour survivors require special educational needs input, and there is often limited scope for these survivors vocationally (Radcliffe et al., 1994). Young adult survivors of childhood cancer typically describe educational difficulties and employment discrimination (Langeveld et al., 2002). Furthermore, Albright and colleagues (1996) found that only 25 per cent of patients in their study who had brain tumours irradiated before their fourth birthdays reached post-secondary education and 33 per cent had never been employed. Given the now-known late effects, much research is focused on devising treatment protocols that avoid or delay the use of radiotherapy without compromising the survival chances of children.

One such intervention programme is the 'Baby Brain' protocol used for the treatment of the third most common paediatric brain tumour, ependymoma (Grundy et al., 2007). Ependymoma was selected because its outcomes are relatively poor in comparison with other brain tumours. Data for ependymoma have revealed a five-year survival rate ranging from 39 to 64 per cent (Grundy et al., 2007; Kulkarni et al., 2004). Furthermore, ependymomas will often require radiotherapy (Grundy et al., 2007), which may lead to the poorer cognitive outcomes mentioned earlier.

The ‘Baby Brain’ protocol was administered to 88 children who were diagnosed with ependymoma under the age of three between 1992 and 2004 in the UK. The premise of this protocol was that, following surgery, a particular chemotherapy strategy was used in order to avoid or delay the use of radiotherapy (Grundy et al., 2007). Importantly, this deferral strategy is not used internationally (Bouffet et al., 2007; Merchant et al., 2004). The intention of this wilful deferral was to evade negative cognitive outcomes without compromising the survival chances of the children diagnosed with ependymoma.

‘Baby Brain’ was successful in its aim to minimise the use of radiotherapy without reducing life expectancy. However, the investigation of subsequent quality of life was not completed, with the capture of neurocognitive data being absent. Consequently, research funded by Candlelighters (a Yorkshire-based children’s cancer charity) is currently being conducted to determine the cognitive and learning outcomes of those survivors of infant ependymoma treated with the described ‘Baby Brain’ deferral protocol. It is hoped a clearer picture of these patients’ cognitive profiles and functioning will now be obtained.

**Contemporary clinical neuropsychological practice**

The need for access to neuropsychological assessment is stated in the 2005 National Institute for Health and Clinical Excellence document for children with cancer (NIHCE, 2005), which talks of ‘using psychological testing and assessment to assay central nervous function and diagnose specific behavioural or cognitive deficits or disorders’ (p.187). Various cognitive domains and learning are examined when trying to assess neuropsychological functioning, such as verbal ability, perceptual reasoning, memory and academic attainment. Standardised assessments may also be used to look at day-to-day functioning as well as communication, social skills and affect. Anticipated cognitive impairments can be revealed, giving an early identification of learning vulnerability and support requirements. Assessment also provides a baseline to monitor future performance. It is important to note that quality of life incorporates not only cognitive and academic outcomes but other key facets, such as physical outcomes and psychosocial functioning (Dennis et al., 2004; Langeveld et al., 2002). Neuropsychological capture alone is not sufficient, and management of adjustment to diagnosis and emotional wellbeing are crucial too. Clearly, this work is a multidisciplinary affair.

Due to the increase in brain tumour survival rates and knowledge of late effects, it is now more important than ever to assess cognition and learning, and its development (Savage et al., 2004). An increase in brain tumour survival rates has

---

**References**


resulted in increasing numbers of children diagnosed with brain tumours within the education system and in wider society (Lahteenmäki et al., 2007), and an increased understanding of the long-term functional impact of treatment becomes imperative (Conklin et al., 2008). It is also critical to further understand differences, as children are affected in diverse ways, depending on factors such as the site of the tumour and age at treatment (Moore, 2005). Early identification and knowledge of these sequelae is vital to reduce or indeed prevent them (Askins & Moore, 2008; Penkman & Scott-Lane, 2007) and determine the longer-term impact of treatments on cognition and learning.

**Provision**

To clarify the current provision of paediatric neuropsychology for neurooncology services within the UK, we conducted a simple survey by e-mailing 39 consultant paediatric oncologists in all 21 paediatric oncology centres and to all UK paediatric neuropsychology services. The survey asked whether any dedicated neuropsychology input was provided, and if so, how much.

The response rate of consultant paediatric oncologists was 44 per cent with 17 of the centres represented. Of the responding centres, 59 per cent had no dedicated neuropsychologists for paediatric neurooncology, 29 per cent had non-dedicated input, 12 per cent (two centres) had 0.4 and 1.0 w.t.e. Neuropsychologists’ response rate was 49 per cent with a centre representation of 69 per cent. More than half of those centres provided no dedicated neuropsychology services. The survey reported that 28 per cent had non-dedicated input and the other three centres ranged from 0.2 to 1.0 w.t.e.

These survey data appear to show inconsistency of provision, with clear implications for the incomplete assessment and capture of cognitive outcomes. There may be great variability in the services that children and families receive.

**Future challenges**

Integrated cognitive and learning assessment offered as a routine part of the clinical process needs to be in place. Services must ensure integration both with the psychological and the neuropsychological. Clinical practice and research may now need to focus on those individuals who are at greatest risk of the adverse cognitive outcomes with earlier assessment and intervention. Moore (2005) has argued that identifying individuals who are at risk is crucial, as disappointingly not every child will experience prospective neuropsychological surveillance as a part of their routine care.

The effects of brain tumours can be devastating. Clinicians want a good understanding of the long-term neuropsychological needs and how best to support the child (Savage et al., 2004). There is also a need to examine which specific parts of neurocognitive interventions make them effective (Limond & Leeke, 2005). Similarly, Rankin and Hood (2005) provide clear and convincing reasons as to why conventional – typically adult-oriented – treatment strategies have limited applicability to children. In addition, they establish a gap between the theories of cognitive development and the actual realities of supporting children with cognitive difficulties.

While much neuropsychological research is understandably directed at the potential of cognitive remediation, we must also remember to evaluate the effect of the ‘scaffolding’ or supportive structures around the child (Meadows, 1996) – for example, quality of support in school.

The survey results discussed earlier indicate the inconsistent and incomplete provision of dedicated neuropsychology for children with brain tumours. This has implications for research too. As time may fail to heal and instead reveals the cognitive and educational needs of children diagnosed with brain tumours, service providers must ensure integrated neuropsychological assessment and further develop a much wanted clinical and research agenda.