

Short Article

Is Methylphenidate Useful to Survivors of Childhood Brain Tumour? An Accessible Summary of Recent Research

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Many children and young people experience long-term difficulties after having a brain tumour. This paper discusses interventions using the medication methylphenidate and describes the current research in this area being conducted at the Great North Children's Hospital (Newcastle upon Tyne) and Newcastle University Centre for Cancer. The children, young people, and their families who use our hospital tell us that some of their most challenging difficulties only happened once the brain tumour treatment had finished. Some survivors of childhood brain tumour are left with lifelong disabilities that result from their cancer or treatment. These disabilities are often related to brain injury, and can be relatively invisible to the general public. Some disabilities only become apparent over the time following treatment. These are known as 'long-term late effects'. The most common long-term late effect that is reported after childhood brain tumour is an acquired brain injury. We see signs of an acquired brain injury following brain tumour in behaviour such as reduced attention, a reduction in ability to remember things, a slowing down of how quickly the child can take in information, and an impact on their academic performance and overall intellectual ability (IQ). Depending on the location of the tumour, brain injury can present in a different way. It is important to remember that the term 'brain injury' refers to any injury affecting the brain, so information on brain injury on the internet may not apply to the specific injury a child has acquired. A child can develop brain injury after a brain tumour due to one or many different factors, including any build-up of fluid in the brain before the tumour was discovered (hydrocephalus), surgery, post-surgical complications (such as posterior fossa syndrome), certain chemotherapies, or radiotherapy. Generally, the younger a child is at the time of diagnosis, the more likely they are to experience significant late effects.

We have worked with a number of patients and their families in Newcastle at the Great North Children's Hospital to help us understand what the role of methylphenidate might be in helping to reduce long-term late effects that affect intellectual and academic ability. Methylphenidate is a medication that is used for a few different reasons. Usually people have heard of methylphenidate by one of its brand names, 'Ritalin', which they know is used for children with Attention Deficit Hyperactivity Disorder (ADHD). We do not use this

for ADHD in our centre, and in fact we do not assess our patients for ADHD. We use this medication to try to reduce the delayed effect on brain function that we see in many children following brain tumour. We read about some research using methylphenidate with children after brain tumour that was carried out in America in 2008 [1-4]. This research found that methylphenidate may be useful for some children and young people who experience late effects after a brain tumour or after acute lymphoblastic leukaemia. We knew that methylphenidate has been trialled also for children and young people who have attentional impairment or slowed cognitive function (slowed thinking speed) after a traumatic brain injury, such as following a serious head injury. We wanted to know what other groups experience was of methylphenidate to help us think about its potential benefit to our patients. We wrote two papers that looked at which other groups of children methylphenidate has been trialled with, and discussed whether these benefits might translate to our patients. Both papers were written with Alexander Hagan, one of our Research Assistants. *Translating Methylphenidate's Efficacy on Selective and Sustained Attentional Deficits to... Childhood Cancer Survivors: A Qualitative Review* [5]. *The Influence of Methylphenidate on Sustained Attention in Paediatric Acquired Brain Injury: A Meta-Analytical Review* [6].

Both of these studies helped us to see that there may be benefit to using methylphenidate as part of more structured clinical use. Methylphenidate has been used in our hospital for patients with traumatic brain injury and with post-cancer brain injury before, but the effects of the medication were not measured fully. Working with our medical colleagues, we started measuring the benefit of methylphenidate with patients at the start of 2017. We have now been working with methylphenidate for nearly seven years and we have published some research about what we have learned. In 2017-2019 we asked children and young people about what *they* thought about using methylphenidate. We collected data on children's views by talking with them and by asking them to complete some short questionnaires with us. We worked with an MSc postgraduate student, Lauren Bell, to help us share our patients' experiences. You can read this in a paper titled "*I feel happy again*": *Methylphenidate Supports Health-Related Quality of Life in Survivors of Paediatric Brain Tumour* [7]. Lauren

looked at questionnaire data that we had collected from 12 of our patients. Analysing these questionnaires, Lauren found that children experienced benefit of methylphenidate in five key areas of life: social, emotional, academic, physical, and cognitive. We also asked parents and carers about their experiences of their child using methylphenidate in 2017-2019. We worked with a doctoral postgraduate student, now Dr Lauren Smith, to write a paper titled *Parental Perceptions of the Efficacy of Methylphenidate on Health-Related Quality of Life in Survivors of Paediatric Brain Tumour* [8]. Lauren gathered questionnaire data that we had collected in clinic from 10 parents/carers. Parents were generally positive about the use of methylphenidate and believed this to have a benefit on their child's quality of life.

From talking with children, young people, and their parents and carers in these parent and patient studies, we learned that post-treatment fatigue was a significant problem in the long term. Patients faced fatigue during treatment, but were experiencing long-term fatigue due to the impact of the tumour and treatment on their cognitive function. We worked with a medical MRes postgraduate, now Dr Jennifer Wood, to look at the impact of fatigue on brain tumour survivors: *Exploring Evidence of Fatigue in Survivors of Pediatric Brain Tumors* [9]. Jenny found that there was a lot of studies that discussed fatigue in cancer survivorship, but many of these were poor quality and did not adequately distinguish between fatigue in the early days related to illness and treatment, and longer term fatigue related to brain injury. A Danish group led by Dr Michael Callesen at Hans Christian Andersen's Children's Hospital are now looking at the effect of methylphenidate on fatigue in children after brain tumour in something called a 'randomised control study'. This sort of study is the gold standard for research as its findings are very robust. We are involved with this study as one of their scientific advisors, and have shared our own research protocol with Dr Callesen's team. We look forward to seeing their results. All the existing research on the use of methylphenidate in cancer survivorship looks at the effects over a relatively short period of time. Most studies only continue for 2-3 weeks. Two studies looked at the impact of methylphenidate over a 12 month period. One of these studies was written by our team: *Methylphenidate Improves Cognitive Function and Health-Related Quality of Life in Survivors of Childhood Brain Tumours* [10]. We looked at anonymised data from 29 patients who were using methylphenidate. We found that methylphenidate had a significant impact on selective attention—that is, the ability to pay attention to a specific stimulus, rather than the other distractions in the room. This is important when listening to a teacher, or trying to pay attention to one's lesson rather than the chatter in the room around one. This study also showed that benefits to quality of life that may be associated with methylphenidate were still present at 12 months.

We wanted to know whether methylphenidate has any benefit on academic attainment and to intellectual ability over the medium to long term. Dr Shauna Palmer explored the factors that cause reduced intellectual ability in long-term survivors of a brain tumour called a medulloblastoma [11]. One of the factors found to be associated with intellectual development was the speed at which an individual can take in information—an area that we know is affected in many survivors of brain tumour. We are interested in finding out whether methylphenidate—used to support the speed at which information is processed—might

decrease the reduction in intellectual ability seen in some survivors. We have just completed writing a case series including six of our patients that have used methylphenidate for over three years: *Key Questions on the Long-Term Utility of Methylphenidate in Paediatric Brain Tumour Survivorship: A Retrospective Clinical Case Series* [12]. This study helped us to identify some unanswered questions about using methylphenidate after brain tumour. We hope to answer many of those questions in our ongoing longitudinal study. This study will run over a further three year period (2022-25) and may help us to answer some of the things that we don't yet know about using methylphenidate with this group. Over the nearly seven years that we have been exploring methylphenidate with our patient group we have learned a lot. We are building experience in identifying which patients are more likely to have mild side-effects and which will be most likely to benefit from the treatment. We still need to discover more about methylphenidate, including gaining more evidence about how long it is useful to take methylphenidate for, and when to stop. We could not do this work without the support of our patients and their families, from whom we are gathering expert data. We look forward to finding out what more we have to learn from our patients, and to being one step closer to making survival from a tumour as positive an experience as possible.

Conflict of Interest

The author claims no conflict of interest.

Statement on Serial Publishing

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