



The Relationship Between Spirituality and the Developing Brain: A Framework for Pediatric Oncology

Rachel S. Werk¹ · David M. Steinhorn² · Andrew Newberg³

© Springer Science+Business Media, LLC, part of Springer Nature 2020

Abstract

Development, whether motor, language, social, or spiritual, is the functional expression of complex brain processes throughout one's life span, the foundations of which are laid in childhood. The effects of cancer, chemotherapy, radiation, and surgical procedures on early brain development have been measured using neuroimaging and developmental assessment tools. We propose that spiritual development may be substantially affected in children with oncological diseases that impact underlying brain processes. By drawing connections between science, spirituality, and medicine, we can better address the spiritual needs of children as they cope with oncological diseases, by mitigating emotional, cognitive, and physical symptoms and improving outcomes.

Keywords Neurodevelopment · Neurotheology · Pediatric oncology · Spirituality

Background

The incidence of childhood cancer has increased by 0.7% per year since 1975 (Siegal et al. 2019). Despite decreasing mortality rates, pediatric cancer still remains one of the leading causes of disease-related death in children ages 1–14 (Davis 2017).

✉ Rachel S. Werk
Rachel.werk@vumc.org

David M. Steinhorn
dsteinhorn@gmail.com

Andrew Newberg
Andrew.newberg@jefferson.edu

¹ Monroe Carell Jr. Children's Hospital at Vanderbilt, Vanderbilt University Medical Center, 2200 Children's Way, Nashville, TN 37232-9760, USA

² Divisions of Pediatric Critical Care and Pediatric Palliative Care, Children's National Medical Center, Washington, DC, USA

³ Department of Integrative Medicine and Nutritional Sciences, Marcus Institute of Integrative Health, Thomas Jefferson University, Philadelphia, PA, USA

Amidst confirming a diagnosis and establishing a treatment plan, spirituality is often overlooked among this population; however, it is important to assess spirituality at time of diagnosis and throughout care (Nelson and Guelcher 2014). Spirituality is defined by the consensus statement as “the aspect of humanity that refers to the way individuals seek and express meaning and purpose and the way they experience their connectedness to the moment, to self, to others, to nature, and to the significant or sacred (Puchalski et al. 2009).”

When reviewing the literature, there have been a limited number of studies that assess spirituality, and specifically, spiritual care implemented in the pediatric oncology patient population. However, this is only part of the picture in assessing spirituality in pediatric oncology patients. We believe that a neurobiological model must also be considered, in conjunction with a spiritual model, to gain a more comprehensive perspective of these children and adolescents. By better understanding the spiritual needs of patients in relation to brain function and development, we, as providers, can provide better supportive care to pediatric oncology patients. In addition, such research may provide the means to mitigate the impact of cancer-directed therapies on emotional, cognitive, and physical symptoms with the goal of improving outcomes in all dimensions of a child’s life. Therefore, we hypothesize that being mindful of the spiritual well-being of the child at neurodevelopmental appropriate levels will improve responses to cancer-directed treatments and enhance quality of life in pediatric oncology patients.

Although a neurological–spiritual approach to human development has been theorized (Newberg and Newberg 2008), this research has not been previously considered within the context of a pediatric oncology population. This article seeks to provide a framework for the development of a neurological–spiritual approach to patient care in pediatric oncology.

Methods

Literature searches were conducted using databases including PubMed, PsycINFO, and Google Scholar with specified search terms including “Spirituality,” “Child Behavior/psychology,” “Brain development,” “Child development,” “Neoplasms/psychology,” “Quality of life,” “Neoplasms/complications,” and “Psychology, Adolescent.” Specific additional articles and references were selected to provide further background or details where needed. As this is a review of existing literature, institutional review was not indicated.

Results and Discussion

Spiritual and Neurological Development in Children

There are limited models upon which to base an integrative approach for spiritual and neurological development. One prominent model was originally developed by James Fowler who pioneered research on assessing spirituality in children through

his framework of faith development over the human lifetime (Fowler 1981). He reflected on the literature's faith development theories to provide a comprehensive approach to spiritual development (Fowler and Dell 2006). He argues that from infancy to age two, humans form trust with caregivers through non-verbal experiences, leading to greater trust and attachment to caregivers. Rituals and dependability further increase this trust and allow for healthy overall development, both psychologically and spiritually, and set the stage for individuals to establish characteristics such as love, strength, and courage, which are vital for establishing a spiritual framework within one's own life (Newberg and Newberg 2008). Spiritual development appears to be associated with neurological development (Newberg and Newberg 2008). Therefore, when attempting to understand spirituality in children, we must also consider neurodevelopmental changes occurring during this time period.

Cerebral metabolic rate of glucose utilization demonstrates a dramatic increase between birth and 4 years of age that more than double adult levels in order to support synaptic proliferation in the cerebral cortex (Chugani 1998). Within the first year of life specifically, these increases in cerebral metabolic rates of glucose utilization are particularly noticeable in the sensorimotor cortex, thalami, brain stem, and cerebellar vermis (Kumar and Chugani 2008). Increased activity can also be seen in the primary visual cortex, parietal and temporal regions, basal ganglia, and cerebellar hemispheres (Chugani and Phelps 1986; Chugani et al. 1987). The increased activity appears to parallel non-language experiences that allow the child to form trust to his/her caregiver and the presence of brain plasticity (Kumar and Chugani 2008).

Lisa Miller argues in her book, *The Spiritual Child*, that all infants have a natural awareness of suffering and a motivation to soothe suffering in others that provides a foundation for spiritual thought processes (Miller 2016). As the child reaches toddlerhood and early childhood (ages 2–6 years old), he/she begins to use language to express thoughts about the world around him/her. The maturation of communication skills provides a framework for evaluating the child's worldly experiences. However, at this stage, reasoning takes on a concrete perspective (as abstract reasoning develops later) (Fowler and Dell 2006). There is an increase in imaginative and creative thinking, with the concept of God included in this type of "magical thinking" process. There is little logical or abstract thought during this early period of development, consistent with reduced metabolism and development of the higher cortical regions of the brain (Newberg and Newberg 2008) as well as lower F-FDG uptake of frontal and temporal lobes compared to the parietal and occipital lobes (Hua et al. 2015).

Upon beginning school, children construct a perspective of one's self and one's world based upon identifying with rituals and stories pertaining to their community. Spiritual thinking in Western societies is often centered on concrete interpretations of stories explained in religion (Newberg and Newberg 2008). There is often an emphasis on ritualistic actions to generate meaning (Miller 2016). By middle childhood (ages 3 to 8 years old), the rise in cerebral glucose utilization that was present in younger childhood remains at a high, greater than twofold the glucose utilization seen in adults sustaining the enhanced connectivity and synapses occurring during

this age (Chugani et al. 1987). Also during this time in childhood, cerebral perfusion studies show that cerebral blood flow and oxygen use are significantly higher than those in adults (Kumar and Chugani 2008). With this enhanced connectivity, children at this stage are still developing their spiritual worldview.

When further assessing which areas of the brain are involved in this development, fractional anisotropy (FA) data show that as age increases, tract volumes in the genu of the corpus callosum follow a quadratic projection (Lebel and Beaulieu 2011). As the genu of the corpus callosum is involved with forging synaptic connections among the frontal cortices (Goldstein and Mesfin 2017), this allows for eventually higher-level cognitive processing as well as spiritual development. The splenium decreases in tract volume with increasing age in ages 5–25 (Lebel and Beaulieu 2011). This decreased tract volume of the splenium of the corpus callosum is involved with decreasing fiber redundancy and increasing complexity in neural associations (Knyazeva 2013) as the child matures both cognitively and spiritually.

Individuals generally enter into a period where they reflect on and expand their world views, allowing for more mature ideologies. By adolescence, the glucose utilization metabolic rate has decreased and mirrors adult values between 16 and 18 years of age (Chugani et al. 1987; Chugani 1994). Also during this time, brain plasticity decreases (Chugani 1994). In general, white matter volume increases from ages 5 to 25, whereas gray matter decreases from ages 5 to 25 (Lebel and Beaulieu 2011). During young adulthood, the overall brain metabolism remains highly stable (Newberg and Newberg 2008) and white matter volume levels off beginning at age 25 (Lebel and Beaulieu 2011). This type of progression and regression of cortical matter both contribute to brain maturation (Toga et al. 2006). Therefore, overall brain volume stays constant during development. From a spiritual standpoint, Fowler describes the synthetic-conventional stage present roughly from adolescence through young adulthood characterized by higher-level operational thinking; however, lacking an ability to perceive a relationship between one's self and others outside of one's own viewpoint (Fowler and Dell 2006).

When assessing specific lobe development, the parietal lobe has prominently been shown to have age-related gray matter loss (Toga et al. 2006). The parietal lobe contains the orientation association area which helps create a sense of one's body in relation to the rest of the world through sensory data processing as well as being involved in religious or spiritual experiences (Newberg 2010). Studies have shown that the parietal lobe will exhibit decreased activity during a spiritual or religious experience (Newberg 2010). Perhaps this is because this sense of self (that is distinct from the surrounding world) is lessened in order to make way for a state of "oneness" with other aspects of the universe. Thus, when speaking of neurodevelopment, as gray matter declines prominently in the parietal lobe, this maturation may affect one's sense of self, and therefore, one's spirituality.

White matter volumetric increases with age are uniformly constant across lobes contemporaneous to spiritual maturation. Researchers have also found that there are age-related increases for the thalamus (functions for emotional memory processing, sensory information relaying, and motor coordination) and decreases for the caudate and globus pallidus (primarily involved in motor coordination and some memory processing) (Brain Development Cooperative Group 2011). It is important to note

that emotional processing is implicated within spiritual development (Newberg 2010) and thus this age-related white matter volume increase within the thalamus coincides with the ongoing spiritual development within an individual.

As the child grows through childhood, adolescence, and adulthood, Fowler emphasizes that later stages of faith development often do not follow a linear trajectory and not everyone transitions from one stage to another. The individuated–reflective stage refers to the period of adulthood when one develops a sense of self-identity and self-worth that extends beyond one’s environment and personal relationships. In adulthood, Fowler argues that other stages of faith can develop such as when an individual comes to terms with other individuals’ differentiating worldviews and beliefs and has a deeper understanding to beliefs and values different from one’s own. Eventually, an individual can enter into a universalizing stage later in life (Fowler and Dell 2006) when an individual delves into a deeper meaning of the world without the biases from differentiating societal factors like race, socioeconomic status, or religion and comes to appreciate a union of one’s self and an ultimate reality (Newberg and Newberg 2008).

It is important to note that this type of spiritual developmental framework mostly coincides with spirituality associated with monotheistic religion and may be different with regard to other religions or spirituality without that type of religious framework.

Spirituality in Pediatric Oncology Patients

When assessing the literature on spirituality in pediatric oncology patients, it is important to note that there is a need to clarify the concept of “spirituality” among this population as there is a lack of consensus across studies researching the topic (McNeil 2016). Often, spirituality is described in conjunction with religiosity and faith. When referring to the concept of spirituality, we will refer to Lisa Miller’s definition of spirituality as it is not necessarily tied to a particular religion (Miller 2016). Newberg and Newberg refer to it as “distinct from religion or religiousness” and less institutionally based (Newberg and Newberg 2008). It has been found that higher spirituality is associated with higher rates of self-related health and life satisfaction among adolescents, whereas religiosity is not associated with an impact on these health constructs (Dankulincova et al. 2018). In the study mentioned, there was no interaction between spirituality and religiosity among this adolescent population, thus demonstrating that spirituality and religiosity are distinct from one another, especially in the context of evaluating one’s health and quality of life.

In a prospective study by Kamper et al. (2010) taking place in Southern California, 60 children ages 6–17 years old diagnosed with advanced cancer were interviewed about their spiritual quality of life using self-reports and healthcare professionals’ reports from the Spiritual Quality of Life Questionnaire. These children either were diagnosed with leukemia that was not responsive to treatment or had relapsed or had a stage 4 solid tumor that had either recurred or progressed. The researchers found that 80% of these children performed some kind of act that made them feel closer to god and often prayed for normalcy. It is interesting for our

purposes to note that there was no difference in choosing to pray based on age with 69% of the 8- to 12-year-old category and 60% of the 13–17-year-olds reporting that they did something that made them feel closer to god. In addition, 74% of the 8–12-year-olds and 81% of the 13–17-year-olds reported that they “prayed” (Kamper et al. 2010). This study did not report further than these descriptive analyses on age; however, this finding may reveal that prayer and feeling closer to a higher power may transcend age and perhaps may be more linked with those dealing with mortality. Another study by Bull and Gillies (2007) included interviewing 5 hospitalized children in Scotland between the ages of 8 and 11 years old with complex health-care needs on their beliefs and ideas about god. They used pictures from a study by Ebmeier et al. (1991) to evoke conversations surrounding beliefs and ideas about god. This population was intended to include different faiths or none at all, and the researchers did not comment which specifically these children practiced. The level of help and power of “god” a hospitalized child within this 8–11-year-old age category ascertained depended on the child’s quality of health. This study was limited however in its small sample size and may not be generalizable to all patients in this population.

Hendricks-Ferguson (2006) analyzed the impact of age and gender on spiritual and religious well-being as well as hope among a sample of adolescents. The sample consisted of adolescents (ages 13–20 years old) diagnosed with a variety of cancers (most notably acute lymphoid leukemia, Hodgkin’s lymphoma, and non-Hodgkin’s lymphoma) recruited from two outpatient settings, an oncology clinic within a Roman Catholic hospital a part of a teaching medical center and a clinic a part of a non-teaching Roman Catholic hospital. Of the adolescents, less than one-half were Roman Catholic, less than 10% did not have any religious affiliation, and the rest acknowledged a variety of different faith backgrounds. This study utilized a cross-sectional design and assessed spiritual well-being through the Spiritual Well-Being Scale (Paloutzian and Ellison 1991). Hope was assessed through the Hopefulness Scale for Adolescents (Hinds 1985). Adolescents in differing age categories reported differing hope and spirituality scores based on gender. Those of the 15–16-year-old age category had more religious well-being scores than those within the 17–20-year-old age category. When analyzing gender differences, Hendricks-Ferguson’s (2006) study found that females reported higher hope and spirituality scores than males with highest hope scores in early adolescent girls aged 13–14 years old and lowest hope scores in early adolescent boys aged 11–14 years old. In terms of spiritual well-being, there were no statistically significant interactions between age and gender. This study is revolutionary as it directly compares spirituality among pediatric oncology patients in terms of age and gender constructs. However, having a convenience sampling from Roman Catholic hospitals with almost half of the sample subscribing to Roman Catholicism may not generalize these data to a larger pediatric oncology population.

In terms of gender differences, a study of 217 undergraduate students at a large mid-western university reported that female college students had increased intrinsic religiosity compared with young men their age according to a self-administered questionnaire asking about levels of religious involvement, beliefs, and feelings of religious devotion (De Haan and Schulenberg 1997). Of this population, about half

of the students identified as Protestant, over a third as Catholic, and about seven percent as no religious affiliation. In addition, 70% of the students were female. Thus, although this population may be skewed in the large majority as self-identifying to a religion, it may be important to note these gender differences when analyzing the effects of a life-threatening illness on spiritual beliefs and attitudes.

When analyzing what is entailed in sustaining motivation and hope during an illness, Woodgate and Degner (2003) found that a key element was the amount and type of support given from a child's family. In this longitudinal interpretive qualitative study, 39 children with cancer (vast majority with leukemia or lymphoma who were 4.5–18 years old) and their families were interviewed through the use of focus groups, formal interviewing techniques, as well as reflexive journaling. Through these processes, the theme of “keeping the spirit alive” emerged which postulated that the participants and their families would not let the cancer experience ruin their “spirit” and helped them get through some of the difficult situations of dealing with cancer. This “spirit” was described as the essence of the participants and their families which helped them overcome hardships. This study offers a unique perspective as to how we define spirituality and the association between a “spirit” and one's own resilience.

Time since diagnosis may also play a role in spiritual well-being as one study found that among adolescents diagnosed with cancer, the highest levels of spiritual well-being were found among those diagnosed less than 2 years compared to those diagnosed 2 or more years (Hendricks-Ferguson 2008). In addition, religious and existential well-being were higher among those diagnosed within a shorter time frame compared to those diagnosed 2–3 years ago. Perhaps these adolescents may rely more heavily on spiritual convictions in order to cope with their initial diagnosis and treatment, side effects of treatment, and uncertainty of remission. Maintaining a stable spiritual outlook can predict long-term psychosocial effects in this population as evidenced by a study that found that finding meaning and peace can predict health-related quality of life in adolescent and young adult cancer survivors after a year, whereas spiritual struggle predicted post-traumatic stress symptoms (Park and Cho 2017). In this longitudinal study, adolescent and young adult (AYA) cancer survivors (ages 15–39 years old) were identified through a cancer registry of a regional hospital to complete two sets of questionnaires scheduled one year apart. Overall, this population had lower spirituality levels than the national average of an AYA sample. Spiritual well-being was measured by a 12-item FACIT-Sp (Peterman et al. 2002), and spiritual struggle was assessed with the Attitudes Toward God Scale-9 (Wood et al. 2010). It is interesting that these researchers found that there was not a significant correlation between time since diagnosis and spirituality as well as with spiritual struggle. Thus, as a survivor, it may not matter how long one has been in remission in order to assess spirituality.

Jones and Weisenfluh (2003) address developmental issues of children who are facing impending death by age-related stages. They claim that at ages 2–5 years old, children can only think concretely and cannot understand temporal relationships such that death is a permanent condition. Children in this age group often believe that their actions cause what happens to them and therefore may not understand that they cannot control their sickness or death. At the 6–11-year-old stage, children have

expanding language skills and social interactions and by age 10 may understand the concept that death involves a permanent condition of never living. By the adolescent stage (12–17 years old), adolescents have formal operational problem-solving abilities and can understand the abstract issues surrounding death and, however, may not fully be developmentally equipped to handle death emotionally, especially as at this time they are struggling between reaching autonomy but still needing to depend on family for support. When analyzing journal entries of a 15-year-old boy living with and eventually succumbing to osteosarcoma in a qualitative study by Flavelle (2011), this boy was noted to grapple with life's meaning and purpose. As he neared the end of his life, his spiritual thoughts became more centered on religion. This centering on religion took the form of praying for strength, reading his bible every day, and mentioning a God that was "protecting him" (Flavelle 2011).

Cancer and Cancer Treatments Affecting Neurological Development Among Pediatric Oncology Patients

It is important when considering how the natural progression of spiritual development changes when children are faced with a life-threatening condition such as cancer, neurological development can be impacted. As more advanced techniques to treat cancers are being discovered and utilized, the effects of chemotherapy and radiation therapy on a pediatric oncology population are still being discovered. It is difficult to quantify the effects of cancer treatments on neurological development among pediatric patients as there are a whole host of malignancies affecting pediatric patients, all requiring different treatment regimens.

For instance, children undergoing chemotherapy for acute lymphocytic leukemia have been shown to have transient white matter abnormalities on MRI as well as neuropsychiatric deficits (Wilson et al. 1991) and cognitive impairment (Kesler et al. 2016). Pediatric patients treated with proton therapy for neurological tumors such as medulloblastoma and craniopharyngioma reported significantly higher IQ scores than those treated with photon therapy (Merchant et al. 2008). Similarly, proton therapy resulted in higher academic reading scores among optic pathway glioma pediatric patients compared to those treated with photon therapy (Merchant et al. 2008).

Medulloblastoma pediatric survivors who underwent whole-brain irradiation have been found to have less frontal and parietal lobe white matter compared with healthy controls and the frontal lobe exhibited much larger differences than the parietal lobe (Qiu et al. 2007). Medulloblastoma patients treated with chemotherapy, radiation, and surgery have been shown to have lower cerebral blood flow compared to children with no neurological or cognitive deficits who exhibit normal brain appearance on MRI (especially exhibiting the largest difference in the thalamus and larger in all gray matter structures compared to white matter structures, except in the nucleus accumbens) (Li et al. 2017). Pilocytic astrocytoma patients treated with surgery alone exhibited similar cerebral blood perfusion as controls (Li et al. 2017). Analysis of animal models found that cranial irradiation on juvenile rats caused long-term depression, whereas in the adult rat brain only caused a reduction in

long-term potentiation in the dentate gyrus of the hippocampus (Zanni et al. 2015). This may show that cranial radiation treatment could have much more deleterious long-term neural plasticity effects in pediatrics compared to adult patients. Acute lymphoblastic leukemia pediatric patients treated with the chemotherapy drug, methotrexate, demonstrated metabolite and white matter changes on MRIs which either resolved or reduced with time (Chu et al. 2003). Pediatric cancer patients prior to oncological treatment with no known evidence of CNS disease demonstrated a gender difference within the 16–17-year-old age group such that females in this group displayed greater cerebral metabolic activity compared to age-matched males (Shan et al. 2014). Interestingly, in this study, Shan and colleagues analyzed this specific population in order to create a framework for analyzing brain development in healthy children (as it is unethical to subject healthy children to unnecessary radiation). They found that PET scans of fluorodeoxyglucose uptake within this population demonstrate similar findings to past studies of healthy children, which then may support the argument that in non-CNS disease, it is the oncological treatment, rather than the non-CNS tumor or bloodstream malignancy that poses neurological risk.

When assessing neurodevelopmental functioning among pediatric oncology patients, Bornstein and colleagues found that compared to healthy controls, children with non-CNS cancers demonstrated motor, mental and language development deficits but were similar in cognitive representational abilities and emotional relationships (Bornstein et al. 2012). Survivors of pediatric low-grade gliomas who underwent surgical resection of their tumor were found to have many ongoing neurocognitive consequences including anxiety, depression, social difficulties, behavioral issues, and suicidal ideation (Turner et al. 2009). Prior to the beginning of treatment, children diagnosed with brain tumors have lower working and verbal memory and attention compared with control children with non-CNS cancer; however, have well preserved perceptual reasoning, processing speed, and verbal comprehension (Margelisch et al. 2015), indicating that the neuropsychological factors within pediatric oncology include not just the tumor itself but the effects of treatment as well.

Neurological–Spiritual Approach to the Pediatric Oncology Population

The field of Neurotheology investigates the complex intersection between the brain and spirituality. The historical foundations of Neurotheology date back thousands of years in Eastern religions, the Bible, and various philosophers over the last 500 years (Newberg 2010). With the advent of modern technology including fMRI and PET imaging, we have discovered complex relationships between spiritual states (such as meditation) and neural changes in cortical networks throughout the parietal cortices, prefrontal cortices, limbic system, and thalamus (Newberg 2010, 2014; Urgesi et al. 2010). We have drawn special attention to the parietal lobe as it includes the orientation association area (which helps shape a sense of self and non-self) and is the site of creating myths (commonly used in spirituality and religion) (d'Aquili et al. 2001). Neurotransmitters serotonin and dopamine have also been implicated in spiritual experiences (Perroud 2009).

By developing and utilizing a neurological–spiritual approach to pediatric oncology, we can better treat this patient population spiritually in relation to their changing neurological function in order to instill a better quality of life, a better understanding of their situation, and perhaps more effective treatment outcomes. We can thus utilize a translational approach of understanding subjective and biological experiences in order to better understand and dictate clinical interventions that can be spiritually oriented.

As all children mature neurologically, the volume of white matter increases, while gray matter decreases as a form of developmental pruning (Lebel and Beaulieu 2011; Toga et al. 2006). This neurological development can be hindered by chemotherapy treatments as certain chemotherapies can result in white matter abnormalities (Wilson et al. 1991; Qiu et al. 2007; Chu et al. 2003). White matter is imperative for healthy brain maturation and to draw cognitive connections (Hagmann et al. 2010), and since neurological development affects spiritual development, this change in white matter development could have consequences on a child's spiritual development. Fowler (1981) indicates in his spiritual development trajectory that children often view the world concretely and over time will develop abstract perspectives and thought. However, if this spiritual trajectory is predicated on neurological development which can be altered with chemotherapy, therefore, pediatric oncology patients may develop an altered spiritual development that coincides with white matter changes.

Although the literature on spirituality in pediatric oncology patients has varied findings, there are studies that support this hypothesis. For instance, researchers have found that the highest levels of spiritual well-being were found among patients those diagnosed less than 2 years compared to those diagnosed two or more years (Hendricks-Ferguson 2008). Another study found that there was not a significant difference for if pediatric oncology patients chose to pray based on age (Kamper et al. 2010) perhaps demonstrating that the effects of cancer and cancer treatments may play a bigger role in prayer and spirituality than one's age, thus disrupting natural spiritual development progression.

Clinical Implications

In the healthy child, spiritual growth and development can follow the developmental constructs outlined in the previous sections of this article. The central issue for clinicians to consider is the practical implications of spiritual development in relation to their neurological development in children who are dealing with healthcare challenges such as cancer. For children with chronic or incurable medical problems, the overarching concern is that normal psycho-physiologic development may not progress as anticipated, due to frequent hospitalizations or developmental disability, leading to failure to appropriately mature. Development also may take on abnormal patterns as ill children attempt to get needs met and achieve emotional security in the often hostile medical environment. It is well recognized that otherwise healthy children experience developmental regression when faced with illness and hospitalization (Li et al. 2016). On the other hand,

we also hear of children with chronic disease being referred to as “old souls,” appearing more sophisticated in their understanding of their disease and life than their healthy peers. Our ability to assess the spiritual development of our pediatric patients is highly dependent on their cognitive and expressive abilities, which give us an indication of what is going on inside their heads and hearts.

Our neurological–spiritual framework to caring for pediatric oncology patients has exciting applications to standards of care within pediatric oncology. Previous studies have addressed the need for spiritual care within pediatric oncology patients and the importance of health care providers’ role in detecting patients’ spiritual needs (McNeil 2016; Lima et al. 2013; Freyer et al. 2006; Feudtner et al. 2003; Hart and Schneider 1997). Specific components of these spiritual needs include finding hope, finding outlets and mediums to be remembered in the event of end of life, express their feelings, and bolster relationships with family members, friends, and a higher power if this is appropriate for that child’s upbringing and environment (Petersen 2014). An intervention implemented within adolescents with cancer to incorporate advance care planning showed increased spirituality scores when compared to controls who did not have advance care planning as well as provided information on when are appropriate times to bring up end-of-life planning (Lyon et al. 2014). Other studies have looked at how the development of personal web pages, creative arts, and guided spiritual imagery have allowed for self-expression (Taylor et al. 2015; Suzuki and Beale 2006). Guidelines have been developed for pediatricians to incorporate assessment of spirituality into their practice, and researchers have advocated a need for incorporating spiritual assessment of patients within medical education (Barnes et al. 2000).

For clinicians caring for children, spirituality in the child must be considered in the context of the family. Children’s concepts of spirituality are shaped by their family’s attitudes toward spirituality, by what they witness in their communities, and by their own experience of it. In contemporary life, more families identify as spiritual rather than religious (Maschi and Lipka 2016; Oppenheimer 2014; Barrie-Anthony 2014), although faith-based communities continue to provide an important foundation for many families. Clinicians must listen carefully for cues from families and should directly ask about the role of faith and spirituality in their lives. Good clinical practice requires a basic spiritual assessment using tools such as the FICA for adults (Puchalski 2014; Puchalski et al. 2018) with engagement of chaplains or the family’s clergyperson when needed. Clinicians who wish to delve deeper into the young child’s spiritual understanding and beliefs, with permission of the parents, can work with child life therapists (previously known as play therapists) or chaplains using non-verbal methods such as drawing a picture of their beliefs and telling stories about the pictures. Children with less expressive ability may benefit from having stories read to them with uplifting spiritual messages relying always on the family’s values and belief system. A clinician should never impose her/his own beliefs on a patient or the family, although many families will ask for the healthcare provider’s opinion. Asking directly about spiritual concerns may give families permission to express hopes, fears, and goals of care (“praying for a miracle” or “knowing that ‘God’ can restore health, if our prayers are strong enough”) (Ferrell et al. 2016). In so doing,

one can align one's clinical care with the family's values and avoid conflict when the family's goals are not consistent with the medical facts.

Research Implications

There is still much to be done within the realm of providing for the spiritual needs for pediatric oncology patients and specifically tailoring neurological changes in conjunction with spiritual needs may prove to be extremely useful. Some studies have already begun to explore this avenue of research in adult breast cancer survivors (Symonds et al. 2011). Future directions of our research include developing studies to investigate our framework such as analyzing fMRI imaging of pediatric oncology patients longitudinally from first diagnosis prior to treatment, during treatment, as well as after treatment in survivorship and/or end of life. We could stratify by age, gender, type of cancer, and type of therapy used to treat their cancers and investigate whether their changing spiritual perspectives correlate with any changes in neural processing and where these neural changes are located. We would match our participants with age- and gender-matched controls who do not have cancer and see how cancer and cancer treatments alter one's neurological development.

Perhaps if we were to create interventions to boost white matter development during certain chemotherapy treatments of pediatric patients, we could affect spirituality in these patients allowing them to continue maturing in their spiritual development. Aerobic fitness has been shown to increase white matter integrity in patients diagnosed with multiple sclerosis (Prakash et al. 2010), and thus, this may be an option in pediatric oncology patients as well. Breast milk promotes white matter growth development in healthy infants (Isaacs et al. 2010) and may be an avenue to pursue in boosting white matter development in pediatric oncology patients. If we can boost spiritual maturation, we can help these patients cope with their illness and worldview more productively, and then when/if they survive, these patients are not stunted in their spiritual development, leading to overall healthier development and increased quality of life (Zebrack and Chesler 2002).

Study Limitations

Limitations of this literature review include the complete dependence on previously published studies and their availability. We recognize that our approach is a speculation based on the literature. As there are many different types of malignancies diagnosed within the pediatric oncology population as well as different treatment modalities for these malignancies, one model may not be generalizable to all pediatric oncology patients. Further, patients with neurological involvement of their cancer (either primary or secondary involvement) may have a differing spiritual development than those without neurological involvement.

A persistent challenge within pediatric medicine for young children arises from the limitations inherent in interpreting their statements and behavioral signs as a reflection of their inner sensations and emotions. One of the primary traits of human

beings is the ability to communicate our thoughts and feelings through words, gestures, pictures, songs, melodies, etc. When people are non-verbal (infants) or neurologically impaired, they lose some aspects of the human quality of communication. If all patients have a spiritual life in a state of good health and verbal competence, then we must try to imagine what the spiritual life is when the individual is unable to communicate. Few authorities would conclude that the human spirit depends upon verbal ability or that it ceases to function simply because an individual loses awareness. This line of reasoning suggests that one's spirituality may be associated with the physical body, perhaps even connected to it in some fashion, but is not the same as the physical body.

Conclusions

Our proposed neurological spiritual model provides a better understanding on the spiritual needs of pediatric oncology patients and the relation to neurological functioning. As spiritual support is fundamental to caring for patients with potential life-limiting conditions such as cancer, this will provide better supportive care to this population in order for them to make sense of their diagnosis and worldview. Past research has shown that integrating a spiritual approach to medical care can not only aid in quality of life and coping with disease but also in positive treatment outcomes (Newberg 2010; Hulett and Armer 2016; Peteet and Balboni 2013; Cotton et al. 2012; Trevino et al. 2010), and thus, it is imperative that we continue to explore this domain. Our research contributes to the broader field of Neurotheology by targeting this specific population and proposing ways to incorporate Neurotheology in clinical practice. By drawing connections between science, spirituality, and medicine, we can better serve the needs of our patients by coping better with illness, optimizing the spiritual self, mitigating emotional, cognitive, and physical symptoms, and hopefully improving treatment outcomes.

Acknowledgements We would like to acknowledge Taeun Chang, M.D., for her thoughtful comments on brain development.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Human and Animal Rights This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent Therefore, informed consent was not needed to conduct this research.

References

- Barnes, L. L., Plotnikoff, G. A., Fox, K., & Pendleton, S. (2000). Spirituality, religion, and pediatrics: Intersecting worlds of healing. *Pediatrics*, 106(Supplement 3), 899–908.

- Barrie-Anthony, S. (2014). 'Spiritual but Not Religious': A rising, misunderstood voting bloc. (No, they're not just atheists.). In *The Atlantic*. <https://www.theatlantic.com/politics/archive/2014/01/spiritual-but-not-religious-a-rising-misunderstood-voting-bloc/283000/>.
- Bornstein, M. H., Scrimin, S., Putnick, D. L., Capello, F., Haynes, O. M., de Falco, S., et al. (2012). Neurodevelopmental functioning in very young children undergoing treatment for non-CNS cancers. *Journal of Pediatric Psychology*, 37(6), 660–673.
- Brain Development Cooperative Group. (2011). Total and regional brain volumes in a population-based normative sample from 4 to 18 years: The NIH MRI Study of Normal Brain Development. *Cerebral Cortex*, 22(1), 1–12.
- Bull, A., & Gillies, M. (2007). Spiritual needs of children with complex healthcare needs in hospital. *Paediatric Nursing*, 19(9), 34.
- Chu, W. C., Chik, K. W., Chan, Y. L., Yeung, D. K., Roebuck, D. J., Howard, R. G., et al. (2003). White matter and cerebral metabolite changes in children undergoing treatment for acute lymphoblastic leukemia: Longitudinal study with MR imaging and 1H MR spectroscopy. *Radiology*, 229(3), 659–669.
- Chugani, H. T. (1994). Development of regional brain glucose metabolism in relation to behavior and plasticity. In G. Dawson & K. W. Fischer (Eds.), *Human behavior and the developing brain* (pp. 153–175). New York, NY: Guilford Publications Inc.
- Chugani, H. T. (1998). Biological basis of emotions: Brain systems and brain development. *Pediatrics*, 102(5), 1225–1229.
- Chugani, H. T., & Phelps, M. E. (1986). Maturation changes in cerebral function in infants determined by 18FDG positron emission tomography. *Science*, 231(4740), 840–843.
- Chugani, H. T., Phelps, M. E., & Mazziotta, J. C. (1987). Positron emission tomography study of human brain functional development. *Annals of Neurology*, 22(4), 487–497.
- Cotton, S., Grosseohme, D., & McGrady, M. E. (2012). Religious coping and the use of prayer in children with sickle cell disease. *Pediatric Blood and Cancer*, 58(2), 244–249.
- d'Aquili, E., Newberg, A., & Rause, V. (2001). *Why God won't go away: Brain science and the biology of belief*. New York: Ballantine.
- Dankulincova Veselska, Z., Jirasek, I., Veselsky, P., Jiraskova, M., Plevova, I., Tavel, P., et al. (2018). Spirituality but not religiosity is associated with better health and higher life satisfaction among adolescents. *International Journal of Environmental Research and Public Health*, 15(12), 2781.
- Davis, K. G. (2017). Pediatric cancer and end-of-life. In L. Berk (Ed.), *Dying and death in oncology* (pp. 147–169). Cham: Springer.
- De Haan, L. G., & Schulenberg, J. (1997). The covariation of religion and politics during the transition to young adulthood: Challenging global identity assumptions. *Journal of Adolescence*, 20(5), 537–552.
- Ebmeier, C., Lough, M. A., Huth, M. M., & Autio, L. (1991). Hospitalized school-age children express ideas, feelings, and behaviors toward God. *Journal of Pediatric Nursing*, 6(5), 337–349.
- Ferrell, B., Wittenberg, E., Battista, V., & Walker, G. (2016). Nurses' experiences of spiritual communication with seriously ill children. *Journal of Palliative Medicine*, 19(11), 1166–1170.
- Feudtner, C., Haney, J., & Dimmers, M. A. (2003). Pediatrics electronic pages-spiritual care needs of hospitalized children and their families: A national survey of pastoral care providers' perceptions. *Pediatrics-English Edition*, 111(1), 192.
- Flavelle, S. C. (2011). Experience of an adolescent living with and dying of cancer. *Archives of Pediatrics and Adolescent Medicine*, 165(1), 28–32.
- Fowler, J. W. (1981). Stages of faith: The psychology of human development and the quest for meaning. Harper & Row. *San Francisco*.
- Fowler, J. W., & Dell, M. L. (2006). Stages of faith from infancy through adolescence: Reflections on three decades of faith development theory. In E. C. Roehlkepartain, P. E. King, L. Wagener, & P. L. Benson (Eds.), *The handbook of spiritual development in childhood and adolescence* (pp. 34–45). SAGE Publications.
- Freyer, D. R., Kuperberg, A., Sterken, D. J., Pastyrnak, S. L., Hudson, D., & Richards, T. (2006). Multidisciplinary care of the dying adolescent. *Child and Adolescent Psychiatric Clinics*, 15(3), 693–715.
- Goldstein, A., & Mesfin, F. B. (2017). *Neuroanatomy, corpus callosum* InStatPearls [Internet]. St. Petersburg: StatPearls Publishing.
- Hagmann, P., Sporns, O., Madan, N., Cammoun, L., Pienaar, R., Wedeen, V. J., et al. (2010). White matter maturation reshapes structural connectivity in the late developing human brain. *Proceedings of the National Academy of Sciences*, 107(44), 19067–19072.

- Hart, D., & Schneider, D. (1997). Spiritual care for children with cancer. *Seminars in Oncology Nursing*, 13, 263–270.
- Hendricks-Ferguson, V. (2006). Relationships of age and gender to hope and spiritual well-being among adolescents with cancer. *Journal of Pediatric Oncology Nursing*, 23(4), 189–199.
- Hendricks-Ferguson, V. (2008). Hope and spiritual well-being in adolescents with cancer. *Western Journal of Nursing Research*, 30(3), 385–401.
- Hinds, P. S. (1985). An investigation of the relationships between adolescent hopefulness, caring behaviors of nurses, and adolescent health care outcomes. *Dissertation Abstracts International*, 46, 2623-B.
- Hua, C., Merchant, T. E., Li, X., Li, Y., & Shulkin, B. L. (2015). Establishing age-associated normative ranges of the cerebral 18F-FDG uptake ratio in children. *Journal of Nuclear Medicine*, 56(4), 575–579.
- Hulett, J. M., & Armer, J. M. (2016). A systematic review of spiritually based interventions and psycho-neuroimmunological outcomes in breast cancer survivorship. *Integrative Cancer Therapies*, 15(4), 405–423.
- Isaacs, E. B., Fischl, B. R., Quinn, B. T., Chong, W. K., Gadian, D. G., & Lucas, A. (2010). Impact of breast milk on intelligence quotient, brain size, and white matter development. *Pediatric Research*, 67(4), 357.
- Jones, B., & Weisenfluh, S. (2003). Pediatric palliative and end-of-life care: Developmental and spiritual issues of dying children. *Smith College Studies in Social Work*, 73(3), 423–443.
- Kamper, R., Van Cleve, L., & Savedra, M. (2010). Children with advanced cancer: responses to a spiritual quality of life interview. *Journal for Specialists in Pediatric Nursing*, 15(4), 301–306.
- Kesler, S. R., Gugel, M., Huston-Warren, E., & Watson, C. (2016). Atypical structural connectome organization and cognitive impairment in young survivors of acute lymphoblastic leukemia. *Brain Connectivity*, 6(4), 273–282.
- Knyazeva, M. G. (2013). Splenium of corpus callosum: patterns of interhemispheric interaction in children and adults. *Neural Plasticity*, 2013, 12.
- Kumar, A., & Chugani, H. T. (2008). PET in the assessment of pediatric brain development and developmental disorders. *PET Clinics*, 3(4), 487–515.
- Lebel, C., & Beaulieu, C. (2011). Longitudinal development of human brain wiring continues from childhood into adulthood. *Journal of Neuroscience*, 31(30), 10937–10947.
- Li, M. D., Forkert, N. D., Kundu, P., Ambler, C., Lober, R. M., Burns, T. C., et al. (2017). Brain perfusion and diffusion abnormalities in children treated for posterior fossa brain tumors. *The Journal of Pediatrics*, 185, 173–180.
- Li, W. H., Chung, J. O. K., Ho, K. Y., & Kwok, B. M. C. (2016). Play interventions to reduce anxiety and negative emotions in hospitalized children. *BMC Pediatrics*, 16(1), 36.
- Lima, N. N., Do Nascimento, V. B., De Carvalho, S. M., Neto, M. L., Moreira, M. M., Brasil, A. Q., et al. (2013). Spirituality in childhood cancer care. *Neuropsychiatric Disease and Treatment*, 9, 1539–1544.
- Lyon, M. E., Jacobs, S., Briggs, L., Cheng, Y. I., & Wang, J. (2014). A longitudinal, randomized, controlled trial of advance care planning for teens with cancer: anxiety, depression, quality of life, advance directives, spirituality. *Journal of Adolescent Health*, 54(6), 710–717.
- Margelisch, K., Studer, M., Ritter, B. C., Steinlin, M., Leibundgut, K., & Heinks, T. (2015). Cognitive dysfunction in children with brain tumors at diagnosis. *Pediatric Blood and Cancer*, 62(10), 1805–1812.
- Maschi, D., & Lipka, M. (2016). Americans may be getting less religious, but feelings of spirituality are on the rise. Retrieved March 1, 2017 from <https://www.pewresearch.org/fact-tank/2016/01/21/americans-spirituality/>.
- McNeil, S. B. (2016). Spirituality in adolescents and young adults with cancer: a review of literature. *Journal of Pediatric Oncology Nursing*, 33(1), 55–63.
- Merchant, T. E., Hua, C. H., Shukla, H., Ying, X., Nill, S., & Oelfke, U. (2008). Proton versus photon radiotherapy for common pediatric brain tumors: Comparison of models of dose characteristics and their relationship to cognitive function. *Pediatric Blood and Cancer*, 51(1), 110–117.
- Miller, L. (2016). *The spiritual child: The new science on parenting for health and lifelong thriving*. New York: Macmillan.
- Nelson, M. B., & Guelcher, C. (2014). Scope and standards of pediatric hematology/oncology nursing practice. In: *Chicago, IL: Association of pediatric hematology oncology nurses*
- Newberg, A. B. (2010). *Principles of neurotheology*. Farnham: Ashgate Publishing Ltd.

- Newberg, A. B. (2014). The neuroscientific study of spiritual practices. *Frontiers in Psychology*, 5, 215.
- Newberg, A. B., & Newberg, S. K. (2008). Hardwired for God: a neuropsychological model for developmental spirituality. In K. K. Kline (Ed.), *Authoritative communities* (pp. 165–186). New York, NY: Springer.
- Oppenheimer, M. (2014). *Examining the growth of the “spiritual but not religious”*. New York: New York Times.
- Paloutzian, R. F., & Ellison, C. W. (1991). *Manual for the spiritual well-being scale*. Nyack, NY: Life Advance.
- Park, C. L., & Cho, D. (2017). Spiritual well-being and spiritual distress predict adjustment in adolescent and young adult cancer survivors. *Psycho-Oncology*, 26(9), 1293–1300.
- Perroud, N. A. (2009). Religion/spirituality and neuropsychiatry. In P. Huguelet & H. Koenig (Eds.), *Religion and spirituality in psychiatry* (pp. 48–64). Cambridge: Cambridge University Press.
- Peteet, J. R., & Balboni, M. J. (2013). Spirituality and religion in oncology. *CA: A Cancer Journal for Clinicians*, 63(4), 280–289.
- Peterman, A. H., Fitchett, G., Brady, M. J., Hernandez, L., & Cella, D. (2002). Measuring spiritual well-being in people with cancer: the functional assessment of chronic illness therapy—Spiritual Well-being Scale (FACIT-Sp). *Annals of Behavioral Medicine*, 24(1), 49–58.
- Petersen, C. L. (2014). Spiritual care of the child with cancer at the end of life: A concept analysis. *Journal of Advanced Nursing*, 70(6), 1243–1253.
- Prakash, R. S., Snook, E. M., Motl, R. W., & Kramer, A. F. (2010). Aerobic fitness is associated with gray matter volume and white matter integrity in multiple sclerosis. *Brain Research*, 1341, 41–51.
- Puchalski, C. M. (2014). The FICA spiritual history tool# 274. *Journal of Palliative Medicine*, 17(1), 105–106.
- Puchalski, C., Ferrell, B., Virani, R., Otis-Green, S., Baird, P., Bull, J., et al. (2009). Improving the quality of spiritual care as a dimension of palliative care: The report of the Consensus Conference. *Journal of Palliative Medicine*, 12(10), 885–904.
- Puchalski, C. M., King, S. D., & Ferrell, B. R. (2018). Spiritual considerations. *Hematology Oncology Clinics*, 32(3), 505–517.
- Qiu, D., Kwong, D. L., Chan, G. C., Leung, L. H., & Khong, P. L. (2007). Diffusion tensor magnetic resonance imaging finding of discrepant fractional anisotropy between the frontal and parietal lobes after whole-brain irradiation in childhood medulloblastoma survivors: reflection of regional white matter radiosensitivity? *International Journal of Radiation Oncology, Biology, Physics*, 69(3), 846–851.
- Shan, Z. Y., Leiker, A. J., Onar-Thomas, A., Li, Y., Feng, T., Reddick, W. E., et al. (2014). Cerebral glucose metabolism on positron emission tomography of children. *Human Brain Mapping*, 35(5), 2297–2309.
- Siegel, R. L., Miller, K. D., & Jemal, A. (2019). Cancer statistics, 2019. *CA: A Cancer Journal for Clinicians*, 69(1), 7–34.
- Suzuki, L. K., & Beale, I. L. (2006). Personal web home pages of adolescents with cancer: Self-presentation, information dissemination, and interpersonal connection. *Journal of Pediatric Oncology Nursing*, 23(3), 152–161.
- Symonds, L. L., Yang, L., Mande, M. M., Mande, L. A., Blow, A. J., Osuch, J. R., et al. (2011). Using pictures to evoke spiritual feelings in breast cancer patients: Development of a new paradigm for neuroimaging studies. *Journal of Religion and Health*, 50(2), 437–446.
- Taylor, E. J., Petersen, C., Oyedele, O., & Haase, J. (2015). Spirituality and spiritual care of adolescents and young adults with cancer. *Seminars in Oncology Nursing*, 31(3), 227–241.
- Toga, A. W., Thompson, P. M., & Sowell, E. R. (2006). Mapping brain maturation. *Focus*, 29(3), 148–390.
- Trevino, K. M., Pargament, K. I., Cotton, S., Leonard, A. C., Hahn, J., Caprini-Faigin, C. A., et al. (2010). Religious coping and physiological, psychological, social, and spiritual outcomes in patients with HIV/AIDS: Cross-sectional and longitudinal findings. *AIDS and Behavior*, 14(2), 379–389.
- Turner, C. D., Chordas, C. A., Liptak, C. C., Rey-Casserly, C., Delaney, B. L., Ullrich, N. J., et al. (2009). Medical, psychological, cognitive and educational late-effects in pediatric low-grade glioma survivors treated with surgery only. *Pediatric Blood and Cancer*, 53(3), 417–423.
- Urgesi, C., Aglioti, S. M., Skrap, M., & Fabbro, F. (2010). The spiritual brain: selective cortical lesions modulate human self-transcendence. *Neuron*, 65(3), 309–319.
- Wilson, D. A., Nitschke, R., Bowman, M. E., Chaffin, M. J., Sexauer, C. L., & Prince, J. R. (1991). Transient white matter changes on MR images in children undergoing chemotherapy for acute

- lymphocytic leukemia: Correlation with neuropsychologic deficiencies. *Radiology*, 180(1), 205–209.
- Wood, B. T., Worthington, E. L., Jr., Exline, J. J., Yali, A. M., Aten, J. D., & McMinn, M. R. (2010). Development, refinement, and psychometric properties of the Attitudes Toward God Scale (ATGS-9). *Psychology of Religion and Spirituality*, 2(3), 148.
- Woodgate, R. L., & Degner, L. F. (2003). A substantive theory of keeping the spirit alive: The spirit within children with cancer and their families. *Journal of Pediatric Oncology Nursing*, 20(3), 103–119.
- Zanni, G., Zhou, K., Riebe, I., Xie, C., Zhu, C., Hanse, E., et al. (2015). Irradiation of the juvenile brain provokes a shift from long-term potentiation to long-term depression. *Developmental Neuroscience*, 37(3), 263–272.
- Zebrack, B. J., & Chesler, M. A. (2002). Quality of life in childhood cancer survivors. *Psycho-Oncology: Journal of the Psychological Social and Behavioral Dimensions of Cancer*, 11(2), 132–141.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.