



Healthy play, better coping: The importance of play for the development of children in health and disease

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ABSTRACT

Play is of vital importance for the healthy development of children. From a developmental perspective, play offers ample physical, emotional, cognitive, and social benefits. It allows children and adolescents to develop motor skills, experiment with their (social) behavioural repertoire, simulate alternative scenarios, and address the various positive and negative consequences of their behaviour in a safe and engaging context.

Children with a chronic or life-threatening disease may face obstacles that negatively impact play and play development, possibly impeding developmental milestones, beyond the actual illness itself. Currently, there is limited understanding of the impact of (1) aberrant or suppressed play and (2) play-related interventions on the development of chronic diseased children. We argue that stimulating play behaviour enhances the adaptability of a child to a (chronic) stressful condition and promotes cognitive, social, emotional and psychomotor functioning, thereby strengthening the basis for their future health. Systematic play research will help to develop interventions for young patients, to better cope with the negative consequences of their illness and stimulate healthy development.

1. Introduction

Play is a highly rewarding activity that is abundant in developing children (Ginsburg et al., 2007; Lillard, 2017). In humans, play is apparent throughout cultures, and it occurs in most non-human mammalian species, as well as in certain birds and reptiles (Ginsburg et al., 2007; Graham and Burghardt, 2010; Lillard, 2017; Pellis and Pellis, 2009). Indeed, in his pivotal work *Homo Ludens: A study of the play-*

element in culture' (1938), historian Johan Huizinga already identified play as one of the most central activities in flourishing societies. From an evolutionary perspective, it is clear that play must serve an important purpose considering the costs it entails in terms of time, energy and risk of injury and predation. Moreover, the fact that play behaviour is widely observed across the animal kingdom (Graham and Burghardt, 2010; Pellis and Pellis, 2009) further highlights its importance for survival. From a developmental perspective, play allows children to

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experiment with their behavioural and social repertoire, and to practice their physical and communication skills. It is therefore assumed that play facilitates the development of social competence, emotional capacities and resilience, creativity and problem-solving skills (Bateson, 2015; Erikson, 1977; Ginsburg et al., 2007; Graham and Burghardt, 2010; Gray, 2009; Habermas and Bluck, 2000; McAdams, 1995; Pellis and Pellis, 2009; Phillips, 2003; Piaget, 1962; Vanderschuren and Trezza, 2014).

A group of children that is likely to display reduced or different forms of play behaviour are children suffering from a chronic somatic disorder (i.e. cystic fibrosis, auto-immune diseases or congenital heart defect) or who have a (current or previous) condition (e.g. premature birth or childhood cancer) with possible life-long consequences. Children with these conditions, to which we will refer as ‘childhood chronic diseases’, are at a significantly increased risk for physical, social, emotional and cognitive problems later in life (Patenaude and Kupst, 2005; Pinquart and Shen, 2011; Pinquart and Teubert, 2012). It is likely that their developmental problems are not only the direct result of their current or previous situation. Functional impairments in physical, social, emotional and cognitive domains are either due to the disease itself (e.g. fatigue, pain), stressful events (e.g. hospitalization, surgery, medical procedures) and/or environmental changes resulting from the condition (e.g. over-anxious parents, social-attachment issues, social interactions with peers). Play behaviour is also impaired in child and adolescent mental disorders, such as depression, anxiety, autism, disruptive behaviour disorders, attention-deficit/hyperactivity disorder (ADHD) and schizophrenia (Alessandri, 1992; Black et al., 1975; Blanc et al., 2005; Edmiston et al., 2015; Helgeland and Torgersen, 2005; Jarrold, 2003; Jones et al., 1994; Jones et al., 2017; Jordan, 2003; Møller and Husby, 2000). Differences in play behaviour amongst these patients have been described as early as during the first year of life (Ungerer and Sigman, 1981; Van Berckelaer-Onnes, 2003), continuing through all phases of play development (Naber et al., 2008), and these may have further long-lasting negative impact on the development of these children. Importantly however, the fact that changes in social interaction and play are often also intrinsically part of the symptom complex of primary psychiatric disorders and not only the result of them, makes it hard to disentangle the contribution of the disease itself and its consequences in this group of children.

This paper focuses on childhood chronic diseases, as their long-lasting negative consequences are likely the result of a reduced possibility for play in these children. We aim to provide an overview of the available evidence and to generate hypotheses on (1) the role of play behaviour in the physical, social, emotional and cognitive development, with a focus on chronically diseased children who are at increased risk for adverse (mental) health outcomes and (2) the use of real-life play, virtual/augmented reality, interactive technologies and applied games as possible interventions to prevent or treat adverse mental health outcomes in relation to childhood chronic diseases.

2. The importance of play for healthy development

2.1. What is play?

Although play is readily recognized by observers, there is currently no formal consensus on a definition of play. Huizinga (1938) described play as ‘a volitional act, within certain limits of space and time, according to voluntarily accepted, but compelling rules, being a goal in itself, accompanied by feelings of excitement and joy, different from everyday life’. Huizinga points to a diversity of play elements in culture and convincingly shows that such elements can be found in games, sports, role-play, theatre, dance, stories, language, poetry, rituals, politics, music, competition, war, knowledge, law, philosophy and art. Indeed, in his seminal work *Philosophical Investigations*, the philosopher Ludwig Wittgenstein (1953) argues that the forms and meanings of play are not separated from each other by sharp boundaries and seem to blend into one another.

More recently, Burghardt and colleagues characterized play from a biological perspective, using five criteria which have striking parallels with Huizinga’s description: play is (1) not fully functional in the context in which it appears, (2) spontaneous, pleasurable, rewarding, and voluntary, (3) different from other more serious behaviours in form (e.g. exaggerated) or timing (e.g. occurring early in life before the more serious version is needed), (4) repeated, but not in unvarying stereotypical form (e.g. rocking or pacing) and (5) initiated in the absence of severe stress (e.g. Graham and Burghardt, 2010). Play is thus usually seen as an activity for enjoyment and recreation rather than for serious or practical purposes. However, although play may appear to have no intended serious or practical purpose, it certainly serves a purpose for those who play. In fact, it is commonly thought that play is important for optimal physical, social, emotional and cognitive child development (Bateson, 2015; Erikson, 1977; Ginsburg et al., 2007; Graham and Burghardt, 2010; Gray, 2009; Habermas and Bluck, 2000; McAdams, 1995; Pellis and Pellis, 2009; Phillips, 2003; Piaget, 1962; Vanderschuren and Trezza, 2014).

2.2. Forms and functions of play in humans and animals

In the absence of a formal definition, descriptions of human play are typically multi-dimensional (Pellegrini and Smith, 1998). Lester and Russel (2008) for example describe five dimensions of play: (1) highly active games such as chasing, rough-and-tumble play and play fighting, (2) pretend and socio-dramatic play, (3) language play, (4) social play and games with rules and (5) and construction play. The National Institute for Play (2018) discerns seven forms of play: (1) attunement or mimic play, (2) body play & movement, (3) object play, (4) social play, (5) imaginative and pretend play, (6) storytelling-narrative play and (7) creative play. This broad variety in forms of play poses a profound challenge to study (the role of) play behaviour objectively and consistently. This may at least partially explain the rather modest body of scientific literature addressing the role of play behaviour in human development – especially in relation to childhood chronic diseases – in contrast to its abundance and important function.

Nevertheless, theories regarding the role of play in humans go back for decades. Erikson (1977) proposed that play allows children to experiment with a wide range of experiences, and simulates their potential real-life consequences. Similarly, Piaget (1962) theorized that make-believe play provides children with opportunities to reproduce real-life conflicts, to work out ideal resolutions for their own pleasure, and to ameliorate negative feelings. Narratives and story-telling can support children in integrating a broad variety of positive and negative life experiences (Habermas and Bluck, 2000). In adolescence, co-constructed narratives have been linked to the development of identity, which is considered a key-element for mental health (McAdams, 1995; Phillips, 2003). Play may also allow for the expression of frustration and rage, allowing the child (or adult) to cope with environmental challenges, thereby contributing to mental health (Sutton-Smith, 2008). Taken together, play allows children to experiment and explore, and playful activities provide a secure setting for testing the consequences of many alternative scenarios, in order to develop a rich and flexible behavioural, social and emotional repertoire. As such, play is a natural tool for children to develop resilience, by learning to cooperate, overcome challenges and negotiate with others. Play in a positive, supportive environment can therefore be considered of crucial importance for the development of children into healthy, competent adults. Importantly, development is not a linear process, and although play is most abundant in children (and young animals), it is present in adults as well. Therefore, play throughout life may serve the development, as well as maintenance (perhaps we should call it ‘continued development’ instead) of physical, social, cognitive and emotional functions (Graham and Burghardt, 2010; Pellis and Pellis, 2009; Sutton-Smith, 2008). Since the thrust of this paper is on the importance of play for children, with a chronic disease, we will focus here on play in the young.

In contrast to the limited research on the role of play in humans, there is a substantially larger body of literature on play in animals (Fagen, 1981; Graham and Burghardt, 2010; Panksepp et al., 1984; Pellis and Pellis, 2009; Vanderschuren et al., 1997, 2016). Animal research allows for more experimental control than research in humans, and because playful behaviour in most animal species is less multifaceted than human play it is easier to recognize and quantify. Like humans, most young mammals spend a substantial amount of time playing. Animal play can be roughly divided into three categories: locomotor play, object play and social play (Burghardt, 1999; Fagen, 1981; Graham and Burghardt, 2010; Pellis and Pellis, 2009). Most of the mechanistic and developmental studies on play have focused on social play behaviour, especially in rats, and these have demonstrated that social play is a highly rewarding activity (Achterberg et al., 2016; Trezza et al., 2009; for review see Trezza et al., 2011). Moreover, there is emerging evidence from rodent studies to support an important role of play behaviour in the development of brain and behaviour (Graham and Burghardt, 2010; Pellis and Pellis, 2009; Špinka et al., 2001; Vanderschuren and Trezza, 2014). Play is thought to be valuable for rehearsing and practicing behaviour required in the adult world, since social play behaviour has similarities in form and structure with adult behaviour in non-play contexts, such as sexual or aggressive behaviours. Albeit apparently similar, youngsters' play is qualitatively different from adult behavioural expressions in that they are initiated by different stimuli, occur in different contexts, are structurally different, and are often fragments of adult animal behaviours (Blanchard and Blanchard, 1977; Graham and Burghardt, 2010; Panksepp et al., 1984; Pellis, 1988; Pellis et al., 1997; Pellis and Pellis, 2005, 2009; Vanderschuren et al., 1997). Because of the structural differences between play and adult behaviour, it is well accepted that the function of play goes beyond the mere training of behavioural skills (e.g. Sutton-Smith, 2008). For example, the initiation of social play behaviour in rats superficially resembles sexual mounting, but it occurs in sexually immature animals, and may be directed at an animal of the same sex (i.e. contextual difference). In addition, the most characteristic behavioural element in rat social play is 'pinning', i.e. one animal lying on its back with the other animal standing over it, which also occurs during aggressive encounters. However, in contrast to aggression, the on-top and on-bottom positions alternate during social play, and the body targets of initiation/ attack differ between social play and aggression: the nape of the neck for the former and rump, flanks, back for the latter (Blanchard and Blanchard, 1977; Pellis, 1988). Importantly, play with others is accompanied or preceded by explicit physical, facial or vocal signals to indicate that the intention of the behaviour is playful in nature, further supporting the notion that play is a separate category of behaviour, rather than primordial sex or aggression (Graham and Burghardt, 2010; Pellis and Pellis, 2009; Sutton-Smith, 2008). Together, this suggests that play behaviour serves to develop physical, social, emotional and cognitive capacities, by varying, repeating, and/or recombining subsequences of behaviour, outside of their primary context (Burghardt, 2005; Graham and Burghardt, 2010; Pellis and Pellis, 2009, 2017; Špinka et al., 2001; Vanderschuren and Trezza, 2014).

3. Play and development in childhood disease

Play is considered essential for the healthy physical, social, emotional and cognitive development of children; it starts in very early childhood (Fig. 1). Yet, children with a chronic or life-threatening disease often face obstacles that negatively impact (possibilities to) play and play development, thus conceivably impeding developmental milestones. First, the developmental challenges of children will be discussed and thereafter, the influence of play will be described.

3.1. Childhood disease and development of mental health problems

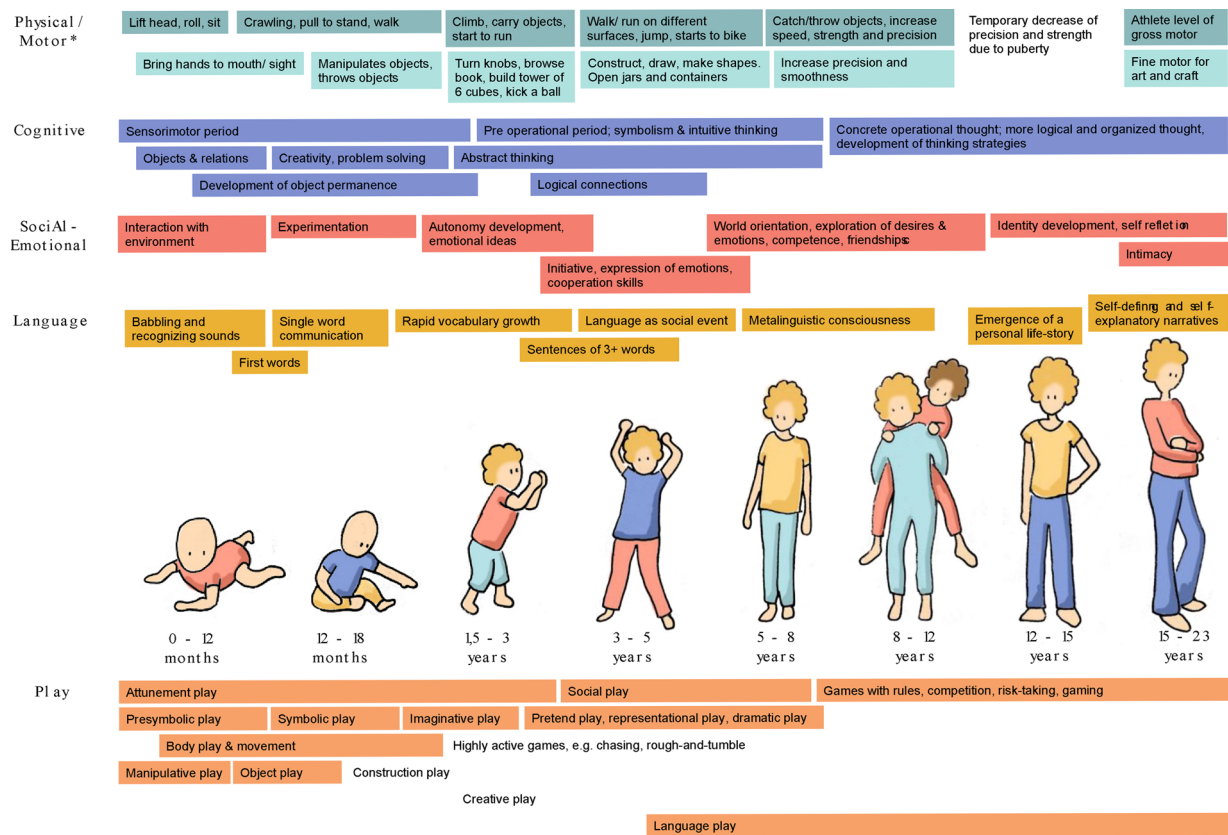
The common definition of chronic disease is comprehensive, i.e. not only encompassing the most prevalent conditions, but all possible ones, somatic as well as psychiatric. Children and youth under the age of 18 with chronic conditions constitute approximately 15% of the Dutch population, amounting to at least 500,000 individuals (Mokkink et al., 2018). In the United States, the rate of children with a chronic condition increased from 12.8% in 1994 to 26.2% in 2006 (Van Cleave et al., 2010). Improving survival rates in somatic childhood disease has been a top priority for researchers, health professionals and policy makers over the last decades. As an impressive result of this joint effort, life expectancy of children with chronic or life-threatening diseases has steadily increased (Perrin et al., 2007; Wise, 2007). However, this prolonged survival comes at a price, i.e. the burden of living every day with a chronic or life-threatening condition (Murray et al., 2013; Perrin et al., 2007; Wise, 2007). Many of these children, adolescents and young adults, remain dependent on medication and healthcare throughout their lives, and may be severely limited in their daily life activities as a consequence of growing up with chronic health problems and long-term co-morbidities (Law et al., 2006; Stam et al., 2006).

Young adults who grew up with a childhood chronic disease have achieved significantly fewer milestones, or at older age than their peers, across different domains (e.g. autonomy, psychosexual and social), as measured using the course of life questionnaire (Grootenhuys et al., 2003). This aberrant development of children with a chronic disease has significant consequences for later functioning and is related to a lower quality of life (Stam et al., 2006). Multiple studies have shown that children with chronic somatic conditions are at a substantially greater risk for poor mental health and social problems compared to their healthy peers. These health issues include depressive symptoms, anxiety, aggression, physical impairment, and problems in academic and social functioning (Patenaude and Kupst, 2005; Pinquart and Shen, 2011; Pinquart and Teubert, 2012). Although psychopathology is not the rule but rather an exception, around 25% of children with a chronic disease encounter psychosocial difficulties (Pinquart and Shen, 2011). Greenham et al. (2015) reported that the susceptibility for mental health and social problems was considerably increased in children with stroke and asthma. Similarly, survivors of childhood cancer have, among others, a higher propensity to develop neurocognitive problems and learning disabilities (Peckham, 1991), as well as difficulties in social functioning (Nijhof et al., 2016; Northman et al., 2015). These problems are, in part, thought to be the result of the (chronic) stress associated with the disease and its consequences.

The impact of childhood disease is not limited to the patients themselves, but often extends to the entire family (Christin et al., 2016; Timko et al., 1993; Vermaes et al., 2012). Chronically diseased children can in turn be affected by parents that experience grief, anger, hopelessness, physical problems, social isolation and financial problems (Cousino and Hazen, 2013; Jackson et al., 2015; Kazak et al., 2015; Poder et al., 2008), which may hamper (possibilities to) play and development, thereby affecting the outcome of the child's illness (Timko et al., 1993; van Gils et al., 2014). In line with this notion, the quality of the home environment (e.g. parent's mental health, affect, communication) has been shown to determine the outcome of chronically diseased children (Greenham et al., 2015). Therefore, the long-term effects of chronic or life-threatening conditions on the development of patients and their families should always be taken into account.

3.2. Challenges of play behaviour in childhood chronic diseases

In addition to the somatic and psychological consequences of their illness, several factors such as isolation, stigma, inequality, bullying and doubts concerning their physical and intellectual capacities are



* Dark: Gross motor skills, Light: Fine motor skills, Frost JL, W ortham SC & Reifel S. Play and Child development 4th ed.(Pearson Education, New Jersey , 2012). The National Institute of Play (www.niplay.org) , Lester, S. & Russel, W. Play for a Change. Play, Policy and Practice: A review of contemporary perspectives. (2008).

Fig. 1. Human play changes during development. Overall scheme of developmental stages and (forms of) play. This is a schematic overview showing appropriate play by age as a development over time. The time frames used are a way of structuring the figure in broad lines, however categories of play are not mutually exclusive and will overlap depending on the child's development, interests and mood. Children may actually alternate between types of play and levels of complexity (Smilansky and Shefatya, 1990) or can be engaged in different categories of play simultaneously (Takhvar and Smith, 1990). Therefore, the figure serves as a broad outline. From 7 years up, play is increasingly influenced by peers (Habermas et al., 2009; McLean, 2005).

Table 1
Some quotes by young people with chronic conditions.

"I remember that I always had to be aware of my arthritis. When other kids played outside, I could not take part." (Young patient with Juvenile Idiopathic Arthritis)
"I am afraid of the blood tests because the collections often go wrong. Therefore, I don't want to go, and hide under my bed." (Young patient with Cystic Fibrosis)
"I always feel as if people cannot help me with any of my problems. This makes me feel anxious, nervous and lonely" (Adolescent with Chronic Fatigue Syndrome)
"Do I participate on the level of an elderly citizen, or should I not participate at all?" (Young patient with Juvenile Idiopathic Arthritis)
"I notice I'm often tired at school and not very social. I realize it's difficult to have many friends, as they prefer talking to more social people. It's also difficult to see them going into town in the school breaks. I can't go with them, because I must consider my energy for the rest of the day. Those are choices I have to make and my classmates don't." (Adolescent with Inflammatory Bowel Disease)

everyday realities for children with chronic diseases (Maes et al., 2017; Pinquart, 2017) that may negatively impact healthy play and development. Being hospitalized, pain and fatigue, social isolation and the 'other-than-normal' treatment of diseased children are likely to compromise their play behaviour. For example, children with leukemia have been shown to play less compared to healthy children (Garipey and Howe, 2003). Moreover, children and adolescents with complex health needs face other significant challenges to participate in normal social activities, because people may respond negatively or in an ambiguous fashion towards them (Green, 2002; Noyes, 2006). Not being able to participate in various social and playful activities puts a strain

on a child's adaptive capacity and resilience, as illustrated by quotes from young patients with various diseases (Table 1). Health care professionals primarily focus on the biological facets of treatment success, and may be less inclined to address the effects of disease on patients' daily routine and self-perceptions. Facilitating and exploiting play in hospitals, as already provided by child life specialists, may therefore prove instrumental in improving the wellbeing and developmental outcome of chronically diseased children.

Given the importance of play for the development of brain and behaviour (Graham and Burghardt, 2010; Pellis and Pellis, 2009; Špinka et al., 2001; Vanderschuren and Trezza, 2014), it is likely that suppressed or aberrant play in chronically diseased children changes their physical, social, emotional and cognitive maturation. However, direct evidence demonstrating the importance of play for healthy development and systematic research focusing on the effects of play on the short- and long-term outcome of chronically diseased children is sparse. Studies that focus on play in chronically diseased children would provide a unique opportunity to learn more about the role of play behaviour in human development. Conversely, optimal strategies, incorporating diverse methodologies such as very early interventions, play therapies, gaming and interactive technology, aimed at improving well-being and quality of life in this population are much needed.

3.3. The challenging environment and play behaviour in children with chronic diseases

In order to properly function and develop across a variety of

domains, children with a chronic disease need to be able to successfully adapt to the challenges of their disease. Here, we argue that there is a relationship between stress, play and resilience in children. Play behaviour can help children with a chronic disease to cope with stress (see Section 4.1). At the same time, stress is well known to hamper play behaviour. Animals that are exposed to severe stress, hunger or disease, presumably compromising their wellbeing, play less (Castelano et al., 2010; Siviý and Panksepp, 1985; Siviý et al., 2006; Siviý and Harrison, 2008; Siviý et al., 2010; Vanderschuren et al., 1995; for review see Held and Špinka, 2011). The sources of stress to which individuals with a past or present childhood (chronic) disease are exposed to are diverse, ranging from stress during hospitalization and treatment regimes to social challenges and physical limitations. Children with a chronic or life-threatening disease may endure painful procedures and frightening treatment experiences as part of medical care (Kazak et al., 2006). Interruption of daily routines, an unfamiliar environment, strange and frightening equipment, and feelings of a lack of control may increase stress in children during hospitalization (Shields, 2001) and can result in a traumatic experience. It is likely that all these factors contribute differently to the negative sequelae of the disease.

Rodent studies show that the absence of play impairs the development of young mammals (for review see Vanderschuren and Trezza, 2014). Rats that were isolated during the developmental phase in which they display most play behaviour, essentially depriving them from social play, develop cognitive deficits such as rigidity and impairments in impulse control and decision making (Baarendse et al., 2013; Einon et al., 1978). Similar play deprivation studies have revealed that social play behaviour is essential for the development of social behaviour. Social play deprived rats exhibit reduced social affiliative behaviour with other rats in adulthood (Hol et al., 1999). Furthermore, when isolated rats are exposed to an aggressive animal in adulthood they are slower to submit than their non-isolated counterparts, and they fail to show normal avoidant behaviour after being socially defeated (van den Berg et al., 1999; Von Frijtag et al., 2002). These findings are in line with the observations of impaired social behavior in monkeys that were raised in isolation and deprived of play (Harlow et al., 1964). Interestingly, Schneider and colleagues used a rodent peer rejection paradigm, essentially depriving playful rats from social interactions by pairing them with non-playful rats. This resulted in deficits in social (play) behaviour, social memory and social transmission of information (Schneider et al., 2014, 2016). These findings are relevant for children with a chronic disease because chronic illness can have detrimental effects on school attendance, relations with peers at school and school engagement. Students with chronic illness demonstrate mixed school experiences and outcomes that are often worse than students without a chronic disease (Lum et al., 2017).

Clearly, there are no human studies that assessed the impact of play deprivation. However, it has been shown that hospitalization and treatment trajectories may cause both physical and social isolation (Pendley et al., 1997; Spirito et al., 1990; Stam et al., 2005, 2006; Vannatta et al., 1998), thereby hampering social play and participation, which have been found to be risk factors for cognitive problems (e.g. Cacioppo and Hawkey, 2009). Interestingly, although children or adolescents with chronic or life-threatening diseases are at risk for adverse outcomes and developmental problems (Pinquart and Shen, 2011), some children appear to thrive in spite of difficult circumstances (Rolland and Walsh, 2006). This apparent inter-individual variation in the long-term outcome of childhood chronic diseases may reflect variability in individuals' adaptive capacity, determined by neurobiological and psychological factors, as well as environmental factors, independent of the disease (e.g. Wallander and Varni, 1998). More knowledge about the potential relation between play behaviour and the vulnerability or resilience to the long-term effects of childhood chronic diseases will be relevant for childhood development at large.

4. Play as an intervention to improve developmental outcomes

Promoting adaptation is critical for children with a chronic disease, who are at risk for adverse outcomes. From a therapeutic perspective, play as intervention is valuable because play: (1) regulates negative affect and diminishes stress, (2) facilitates coping with adverse events, (3) is useful for processing new information both cognitively and emotionally by allowing for order and integration, (4) is a safe way to practice new behaviour and experiment with solutions, (5) stimulates fantasy and creative (divergent) thinking and (6) stimulates the development of empathy (Groothoff, 2010). To develop effective play interventions, there is a need for longitudinal studies into the contribution of play to coping skills and the development of children with a chronic disease. Moreover, the complex relationship between the physical, social, emotional and cognitive consequences of the disease should be taken into account.

4.1. Play in paediatric (hospital) care

In paediatrics, play is commonly used to support existing treatment programs and paediatric (hospital) care, although only a few studies have specifically focused on the impact of play on treatment outcomes. Applied as a mediator, play may enhance social contact and reduce anxiety and depression, thus reducing the psychopathology and subsequent fatigue often reported by children with a chronic disease. For example, a study in Brazil showed that playful communication with children about their chronic illness resulted in better coping with the disease (de Moura et al., 2014). Moreover, play has been shown to reduce pain and anxiety in children with burn injuries (Moore et al., 2015).

Child life specialists support children during their treatment in an age appropriate manner, to reduce medical related traumatic stress by, for example, preparing them for medical procedures and teaching them adequate coping strategies (Cole et al., 2001). They use play in various ways to help children cope with their disease, treatment regimes and hospitalization. Potasz et al. for example studied the use of unstructured play as an intervention to help hospitalized children cope with stress. In a randomized clinical trial, they found that children between 7–11 years old showed lower cortisol levels after participating in play activities (Potasz et al., 2013), suggesting that play can reduce stress, even in a highly stressful context like a hospital. Moreover, this implies that a hospitalization period should, if possible, not interrupt play routines in a child's life, since play activities may help the child to identify a similarity with his/her life outside the hospital, making it easier to adapt to a hospital stay.

These examples are by no means an exhaustive overview of current evidence-based interventions. It is clear that the field of play interventions in children with chronic conditions is still very much in development and that more and better (evidence based) interventions are needed. Considering the ever more prominent focus on longitudinal, lifespan paediatric care, it could be argued that early interventions should actually focus more on emotional development through play, thereby integrating skills such as speech, motor and cognitive skills, rather than focusing on these skills in isolation. Safe-guarding and managing the mental health of infants lays the basis for healthy development, thereby laying the foundation for greater social, emotional and intellectual capacities. For older children, our recent studies show that skills training, e.g. sports or social interactions, in a playful setting improves the ability of patients to cope with their disease (van Brussel et al., 2011). Based on such findings, group-based prevention programs – focusing on the integration of bodily self-awareness, emotional self-experience and social interaction through play and sports – have now been structurally implemented in the care for children aged 8–12 years with chronic conditions (UMCU and WKZ sportief, 2017). Other

examples are games that have been applied to enhance coping and provide psycho-education such as the haemophilia coping and perception test (HCPT) and Shoptalk (Limperg et al., 2015; Wiener et al., 2011).

4.2. Treatment potential of game technology

Modern technology has led to a profound change in play behaviour of children. The average 8–14 year old spends more than one hour per day playing video games (Rideout et al., 2010; Van der Geest et al., 2017), accumulating to at least 10,000 h of play by the age of 21 (McGonigal, 2011). Applied games are video games used for non-leisure purposes. They hold immense potential to train and teach new forms of thoughts and behaviour, as well as to address specific behavioural domains. Indeed, recent studies have used applied games to successfully decrease anxiety or depressive symptoms in adolescents (Fleming et al., 2012, 2017; Lau et al., 2017; Merry et al., 2012; Poppelaars et al., 2016; Scholten et al., 2016; Schuurmans et al., 2015; van Rooij et al., 2016; Wijnhoven et al., 2015).

Playing games can influence social, emotional and cognitive development. The immersive social context of today's games help gamers rapidly learn social skills and pro-social behaviour (Granice et al., 2014). Indeed, playing a prosocial game was shown to induce long-lasting enhancements in e.g. helping, cooperation, empathy and emotional awareness (Gentile et al., 2009). Moreover, individuals who had played a cooperative game showed more prosocial behaviour in a dilemma task than players who had played competitively (Ewoldsen et al., 2012), suggesting that these behaviours might be transferable to their peer and family relations outside the gaming environment. Playing games may also affect emotion processing, for both positive (Fredrickson, 2001) and negative emotions (Gottman, 1986). Just as with regular play, video games can be real enough to make the accomplishments of goals matter, but are also safe enough to practice skills to control or modulate negative emotions to achieve those goals (Granice et al., 2014). Little is known about the long-term effects of gaming on emotions and mood, although there are reasons to think that gaming may be positive for an individual's growth and social connection. For example, several studies have reported improved perceived mood in individuals after playing games (e.g. Russoniello et al., 2009; Ryan et al., 2006). Furthermore, playing video games can enhance problem solving skills and creativity (Adachi and Willoughby, 2013; Jackson et al., 2012) and, mostly action games, have a positive impact on focus and spatial skills (Green and Bavelier, 2012; Uttal et al., 2013). In addition, a recent study on the consequences of playing video games, identified positive outcome for intellectual functioning, competence in reading, mathematics, spelling and academic achievement (Kovess-Masfety et al., 2016). These positive effects are transferable to tasks outside the video game, and cognitive training in one domain is known to also have positive effects on performance in other domains (e.g. Bickel et al., 2011).

What if these playful interactions were also training skills that prevent or treat (mental) health problems such as anxiety disorders or disabling fatigue, whilst at the same time circumventing the limitations of physical play interventions? Regular video games can positively influence the health and healthcare of patients. On the one hand, games can be used to distract patients and help them to cope with the side effects of treatments, like nausea, vomiting, anxiety, fatigue and pain, much the same as physical play does (Moore et al., 2015). On the other hand, regular games can be used to motivate and engage patients in physical activity and therapy as well. For example, playing video games has been shown to reduce conditioned nausea of diseased children (Redd et al., 1987; Vasterling et al., 1993) and children show reduced anxiety when they were allowed to play with a Gameboy prior to and during the induction of anaesthesia (Patel et al., 2006). These findings suggest that computer games may have the same effect as an – often more expensive – relaxation training. Games also have the potential to

enhance mental health and wellbeing in children and adolescents (Ferguson and Olson, 2012; Granice et al., 2014; Lobel et al., 2014). For example, Merry et al. found that the video game 'SPARX' was effective in reducing depressive symptoms among adolescents (2012). They concluded that it was a potential alternative for the usual care for adolescents with depressive symptoms in primary care settings and that it could be used to address some of the unmet demands for treatment. More recently, the applied game Mindlight (developed by the Playnice Institute) was shown to significantly reduce anxiety in children with anxiety disorders (Schoneveld et al., 2016). However, no studies to date have investigated the effect of applied games on depressive or anxiety symptoms of children with a chronic disease, although there is increasing attention in the paediatric setting for (applied) games and the use of apps. Indeed programs, such as Cogmed, have been shown to increase cognitive outcomes in childhood cancer survivors (Cox et al., 2015) and serious games have been developed to support medical education (e.g. Charlier et al., 2016; Drummond et al., 2017; Olszewski and Wolbrink, 2017).

Due to the fact that games are very engaging and motivational, playing games may increase adherence to the required treatment procedures. As such, video games can also be a successful adjunct to existing therapy (Kato et al., 2008; Kato, 2010). Enhanced treatment compliance through the application of video games was first shown using the game Re-Mission (Tate et al., 2009). Modern technology has also led to a new type of gameplay in which the users are forced to be physically active as part of the game play. For example, the Nintendo Wii with certain accessories requires the users to be physically active to achieve certain goals in the game. Although certain games cannot be compared to real physical activity as in sports, it has been shown that it leads to an increased energy expenditure when compared to inactive and sedentary games (Graves et al., 2008; Lanningham-Foster et al., 2006). Other games, such as Need for Speed 2 and Power Boat Racer, positively influence the activity of patients with physical impairments, thereby enhancing the chances of treatment success (Kato, 2010). Still, in the systematic research on chronic childhood disease, playing, gaming and interactive technology remain a largely uncharted scientific territory.

Taken together, these studies underscore the potential of game interventions in chronically diseased children, provided they are sufficiently appealing. Applied games could be combined with patient-tailored tools to assess a patient's wellbeing in dedicated e-health platforms to deliver personalized interventions. A broad implementation of e-health applications, aimed at (personalized) prevention and intervention strategies, has the potential to be a cost-effective instrument to increase social participation and optimal development of chronically diseased children.

5. Conclusions and future directions in play research

Investigating the broader issues described in this paper will be of crucial importance to develop theoretically sound, practically relevant, and truly implementable strategies, directly beneficial for young people with chronic conditions and their families. Play interventions, either real-life, digital, or combined, have clear potential to enhance physical, social, emotional and cognitive development. As such, they hold great promise for both preventive and treatment strategies directed at psychosocial problems of children with chronic or life-threatening diseases. However, the complexities of studying play poses major challenges in methodically measuring inter-individual differences in play behaviour, and the need for the development of personalized play interventions is obvious. This warrants interdisciplinary research on play behaviour – as it relates to the optimal healthy development of children and adolescents with a chronic somatic condition – focusing on the following three aspects.

First, in order to enable a systematic monitoring and analysis of play behaviour in relation to physical, social, emotional and cognitive

development, innovative longitudinal measurements and life-span designs are needed. Such measurements cannot only revolve around traditional questionnaires and observational methodologies (Eggum-Wilkens et al., 2014; Jones et al., 2017), but will increasingly depend on the development of new, age-appropriate, automated individual measures of unstructured free, as well as rule-based play dynamics in social groups, such as tagging (Moreno Celleri and Poppe, 2016). Systematic research on the role of play in the development of chronically diseased children will help to assess vulnerabilities and resilience among this population. Moreover, it will help to identify the behavioural factors that could be targeted to support a healthy developmental outcome for future generations.

Secondly, more systematic large-scale studies are needed to assess and develop effective play-based preventive and treatment options for young patients with chronic conditions, through real-life training-programs, virtual reality approaches or gaming interventions. Moreover, an important daily reality for children and adolescents with chronic diseases is that their symptoms (e.g. pain and fatigue) and the long-lasting intensive treatments often limit their participation in peer, family, school, and physical activities, which can result in unwanted social exclusion. While the challenges of physical play may be circumvented using applied games, one could argue that these may not be able to entirely substitute for real-life physical and social play. Innovative play-based strategies addressing the possible societal consequences of chronic childhood diseases should therefore also promote social inclusion by encouraging the enduring interaction with healthy peers. Thus, it will be of increasing interest to study whether young patients can be enabled to rise above the physical, social, emotional and cognitive limitations of their conditions by participating in play with their healthy peers in augmented realities – for example through technology-assisted interactive playgrounds (Moreno Celleri and Poppe, 2016) or applied gaming.

Third, more knowledge about play behaviour and the development of children with a chronic disease can be used to develop and improve educative means to raise awareness about chronic childhood disease, for example to increase awareness about depression (Plechawska-Wójcik and Jakub, 2015). This may reduce social isolation and enhance interactive play between healthy and diseased peers. Understanding the impact of aberrant play behaviour in chronic childhood disease will also provide more insight in the role of play behaviour in human development in general. Moreover, although there is much focus on vulnerability of children with a chronic disease and their increased risk for developmental problems, a substantial group of young patients (and their families) adapt effective strategies to mitigate the physical and psychosocial obstacles they face; they display an impressive resilience potency. Therefore, by systematically studying neurobiological and psychological determinants of stress resilience that enable these patients to adapt to the physical, social, emotional and cognitive challenges of life, much might be learned about adolescents' adaptive capacities, from which all adolescents may benefit in their healthy development.

The abovementioned research directions will entail a paradigm shift from a weakness and dysfunction-oriented approach to a more strength and capabilities-based approach in promoting children's well-being (Franssen and Van Geelen, 2017; Seligman, 2002). The advantages of investigating play in relation to healthy development are clear: it promotes the well-being and quality of life and serves a strong basis for future health of young patients with chronic conditions and their families, and converges with the prospect of a more meaningful and inclusive society, and a more efficient and cost-effective healthcare system.

Authors' contributions

SN and HL are the primary investigators on this review. SN, HL, CV, SvG and SD drafted the manuscript. Cvde, LV and RE developed the

theoretical framework. All authors provided critical feedback and helped shape the manuscript.

Competing interest

The authors declare that they have no competing interests.

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References

- Achterberg, E.J., van Kerkhof, L.W., Servadio, M., van Swieten, M.M., Houwing, D.J., Aalderink, M., Driel, N.V., Trezza, V., Vanderschuren, L.J.M.J., 2016. Contrasting roles of dopamine and noradrenaline in the motivational properties of social play behavior in rats. *Neuropsychopharmacology* 41, 858–868.
- Adachi, P.J., Willoughby, T., 2013. More than just fun and games: the longitudinal relationships between strategic video games, self-reported problem solving skills, and academic grades. *J. Youth Adolesc.* 42, 1041–1052.
- Alessandri, S.M., 1992. Attention, play, and social behavior in ADHD preschoolers. *J. Abnorm. Child Psychol.* 20, 289–302.
- Baarendse, P.J., Counotte, D.S., O'Donnell, P., Vanderschuren, L.J.M.J., 2013. Early social experience is critical for the development of cognitive control and dopamine modulation of prefrontal cortex function. *Neuropsychopharmacology* 38, 1485–1494.
- Bateson, P., 2015. Playfulness and creativity. *Curr. Biol.* 25, R12–16.
- Bickel, W.K., Yi, R., Landes, R.D., Hill, P.F., Baxter, C., 2011. Remember the future: working memory training decreases delay discounting among stimulant addicts. *Biol. Psychiatry* 69, 260–265.
- Black, M., Freeman, B.J., Montgomery, J., 1975. Systematic observation of play behavior in autistic children. *J. Autism Child. Schizophr.* 5, 363–371.
- Blanc, R., Adrien, J.L., Roux, S., Barthelemy, C., 2005. Dysregulation of pretend play and communication development in children with autism. *Autism* 9, 229–245.
- Blanchard, R.J., Blanchard, D.C., 1977. Aggressive behavior in the rat. *Behav. Biol.* 21, 197–224.
- Burghardt, G.M., 1999. Play. In: Greenberg, G., Haraway, M.M. (Eds.), *Comparative Psychology: A Handbook*. Garland Publishing Co., New York, pp. 725–735.
- Burghardt, G.M., 2005. *The Genesis of Animal Play Testing the Limits*. MIT Press, Cambridge, MA.
- Cacioppo, J.T., Hawkey, L.C., 2009. Perceived social isolation and cognition. *Trends Cogn. Sci. (Regul. Ed.)* 13, 447–454.
- Castelhano, A.S., Scorza, F.A., Teixeira, M.C., Arida, R.M., Cavalheiro, E.A., Cysneiros, R.M., 2010. Social play impairment following status epilepticus during early development. *J. Neural Transm.* 117, 1155–1160.
- Charlier, N., Zupancic, N., Fieuws, S., Denhaerynck, K., Zaman, B., Moons, P., 2016. Serious games for improving knowledge and self-management in young people with chronic conditions: a systematic review and meta-analysis. *JAMIA* 23, 230–239.
- Christin, A., Akre, C., Berchtold, A., Suris, J.C., 2016. Parent-adolescent relationship in youths with a chronic condition. *Child Care Health Dev.* 42, 36–41.
- Cole, W., Diener, M., Wright, C., Gaynard, L., 2001. Health care professionals' perceptions of child life specialists. *Child. Health Care* 30, 1–15.
- Cousino, M.K., Hazen, R.A., 2013. Parenting stress among caregivers of children with chronic illness: a systematic review. *J. Pediatr. Psychol.* 38, 809–828.
- Cox, L.E., Ashford, J.M., Clark, K.N., Martin-Elbahesh, K., Hardy, K.K., Merchant, T.E., Ogg, R.J., Jeha, S., Willard, V.W., Huang, L., Zhang, H., Conklin, H.M., 2015. Feasibility and acceptability of a remotely administered computerized intervention to address cognitive late effects among childhood cancer survivors. *Neurooncol. Pract.* 2, 78–87.
- de Moura, F.M., Junior, A.L., de Dantas, M.S., Araujo Gda, C., Collet, N., 2014. Playful intervention with chronically-ill children: promoting coping. *Rev. Gaucha Enferm.* 35, 86–92.
- Drummond, D., Monnier, D., Tesniere, A., Hadchouel, A., 2017. A systematic review of serious games in asthma education. *Pediatr. Allergy Immunol.* 28, 257–265.
- Edmiston, E.K., Merkle, K., Corbett, B.A., 2015. Neural and cortisol responses during play with human and computer partners in children with autism. *Soc. Cogn. Affect. Neurosci.* 10, 1074–1083.
- Eggum-Wilkens, N.D., Fabes, R.A., Castle, S., Zhang, L., Hanish, L.D., Martin, C.L., 2014. Playing with others: head start children's peer play and relations with kindergarten school competence. *Early Child. Res. Q.* 29, 345–356.
- Einon, D.F., Morgan, M.J., Kibbler, C.C., 1978. Brief periods of socialization and later behavior in the rat. *Dev. Psychobiol.* 11, 213–225.
- Erikson, E.H., 1977. *Toys and Reason: Stages in the Ritualization of Experience*. W. W. Norton & Company, New York.
- Ewoldsen, D.R., Eno, C.A., Okdie, B.M., Velez, J.A., Guadagno, R.E., DeCoster, J., 2012. Effect of playing violent video games cooperatively or competitively on subsequent cooperative behavior. *Cyberpsychol. Behav. Soc. Netw.* 15, 277–280.
- Fagen, R.M., 1981. *Animal Play Behavior*. Oxford University Press, New York and Oxford.
- Ferguson, C.J., Olson, C.K., 2012. Friends, fun, frustration and fantasy: child motivations

- for video game play. *Motiv. Emot.* 37, 154–164.
- Fleming, T., Dixon, R., Frampton, C., Merry, S., 2012. A pragmatic randomized controlled trial of computerized CBT (SPARX) for symptoms of depression among adolescents excluded from mainstream education. *Behav. Cogn. Psychother.* 40, 529–541.
- Fleming, T.M., Bavin, L., Stasiak, K., Hermansson-Webb, E., Merry, S.N., Cheek, C., Lucassen, M., Lau, H.M., Pollmuller, B., Hetrick, S., 2017. Serious games and gamification for mental health: current status and promising directions. *Front. Psychiatry* 7, 215.
- Franssen, G.E.H.I., Van Geelen, S.M., 2017. Self-management as management of the self: future directions for healthcare and the promotion of mental health. *Philos. Psychiatr.* 24, 179–184.
- Fredrickson, B.L., 2001. The role of positive emotions in positive psychology. The broaden-and-build theory of positive emotions. *Am. Psychol.* 56, 218–226.
- Garipey, N., Howe, N., 2003. The therapeutic power of play: examining the play of young children with leukaemia. *Child Care Health Dev.* 29, 523–537.
- Gentile, D.A., Anderson, C.A., Yukawa, S., Ihori, N., Saleem, M., Lim, K.M., Shibuya, A., Liau, A.K., Khoo, A., Bushman, B.J., Rowell Huesmann, L., Sakamoto, A., 2009. The effects of prosocial video games on prosocial behaviors: international evidence from correlational, longitudinal, and experimental studies. *Pers. Soc. Psychol. Bull.* 35, 752–763.
- Ginsburg, K.R., American Academy of Pediatrics Committee on, C, American Academy of Pediatrics Committee on Psychosocial Aspects of, C, Family, H., 2007. The importance of play in promoting healthy child development and maintaining strong parent-child bonds. *Pediatrics* 119, 182–191.
- Gottman, J.M., 1986. In: Parker, J.M.G.J.G. (Ed.), *The World of Coordinated Play: Same-and Cross-Sex Friendship in Young Children*. Cambridge University Press, New York, NY, US, pp. 139–191.
- Graham, K.L., Burghardt, G.M., 2010. Current perspectives on the biological study of play: signs of progress. *Q. Rev. Biol.* 85, 393–418.
- Granic, I., Lobel, A., Engels, R.C., 2014. The benefits of playing video games. *Am. Psychol.* 69, 66–78.
- Graves, L., Stratton, G., Ridgers, N.D., Cable, N.T., 2008. Energy expenditure in adolescents playing new generation computer games. *Br. J. Sports Med.* 42, 592–594.
- Gray, P., 2009. Play as a foundation for hunter-gatherer social existence. *Am. J. Play* 1, 476–522.
- Green, S.E., 2002. Mothering Amanda: musings on the experience of raising a child with cerebral palsy. *J. Loss Trauma* 7, 21–34.
- Green, C.S., Bavelier, D., 2012. Learning, attentional control, and action video games. *Curr. Biol.* 22, R197–206.
- Greenham, M., Hearps, S., Gomes, A., Rinehart, N., Gonzalez, L., Gordon, A., Mackay, M., Lo, W., Yeates, K., Anderson, V., 2015. Environmental contributions to social and mental health outcomes following pediatric stroke. *Dev. Neuropsychol.* 40, 348–362.
- Grootenhuys, M.A., Stam, H., Destrée-Vonk, A., Last, B.F., 2003. Levensloop Vragenlijst voor Jong-Volwassenen [Course of Life questionnaire for young adults]. *Gedrag Gezond.* 31, 336–350.
- Groothoff, E., 2010. Inleiding: de plaats van spelpsychotherapie in het veld. In: Groothoff, E., Jamin, H., de Beer-Hoefnagels, E. (Eds.), *Spel in Psychotherapie. Theorie, Techniek En Toepassing*. Koninklijke Van Gorcum, pp. 3–15.
- Habermas, T., Bluck, S., 2000. Getting a life: the emergence of the life story in adolescence. *Psychol. Bull.* 126, 748–769.
- Habermas, T., Ehler-Lerche, S., de Silveira, C., 2009. The development of the temporal macrostructure of life narratives across adolescence: beginnings, linear narrative form, and endings. *J. Pers.* 77, 527–559.
- Harlow, H.F., Rowland, G.L., Griffin, G.A., 1964. The effect of total social deprivation on the development of monkey behavior. *Psychiatr. Res. Rep.* 19, 116–135.
- Held, S.D.E., Spinka, M., 2011. Animal play and animal welfare. *Anim. Behav.* 81, 891–899.
- Helgeland, M.I., Torgersen, S., 2005. Stability and prediction of schizophrenia from adolescence to adulthood. *Eur. Child Adolesc. Psychiatry* 14, 83–94.
- Hol, T., Van den Berg, C.L., Van Ree, J.M., Spruijt, B.M., 1999. Isolation during the play period in infancy decreases adult social interactions in rats. *Behav. Brain Res.* 100, 91–97.
- Huizinga, J., 1938. *Homo Ludens: a Study of the Play-element in Culture*. Routledge, Switzerland.
- Jackson, L.A., Witt, E.A., Games, A.I., Fitzgerald, H.E., von Eye, A., Zhao, Y., 2012. Information technology use and creativity: findings from the Children and Technology Project. *Comput. Hum. Behav.* 28, 370–376.
- Jackson, A.C., Crydenberg, E., Liang, R.P., Higgins, R.O., Murphy, B.M., 2015. Familial impact and coping with child heart disease: a systematic review. *Pediatr. Cardiol.* 36, 695–712.
- Jarrold, C., 2003. A review of research into pretend play in autism. *Autism* 7, 379–390.
- Jones, P., Rodgers, B., Murray, R., Marmot, M., 1994. Child development risk factors for adult schizophrenia in the British 1946 birth cohort. *Lancet* 344, 1398–1402.
- Jones, R.M., Pickles, A., Lord, C., 2017. Evaluating the quality of peer interactions in children and adolescents with autism with the Penn Interactive Peer Play Scale (PIPPS). *Mol. Autism* 8 28-017 0144-x. eCollection 2017.
- Jordan, R., 2003. Social play and autistic spectrum disorders: a perspective on theory, implications and educational approaches. *Autism* 7, 347–360.
- Kato, P.M., 2010. Video games in health care: closing the gap. *Rev. Gen. Psychol.* 14, 113–121.
- Kato, P.M., Cole, S.W., Bradlyn, A.S., Pollock, B.H., 2008. A video game improves behavioral outcomes in adolescents and young adults with cancer: a randomized trial. *Pediatrics* 122, e305–317.
- Kazak, A.E., Kassam-Adams, N., Schneider, S., Zelikovsky, N., Alderfer, M.A., Rourke, M., 2006. An integrative model of pediatric medical traumatic stress. *J. Pediatr. Psychol.* 31, 343–355.
- Kazak, A.E., Schneider, S., Didonato, S., Pai, A.L., 2015. Family psychosocial risk screening guided by the Pediatric Psychosocial Preventative Health Model (PPPHM) using the Psychosocial Assessment Tool (PAT). *Acta Oncol.* 54, 574–580.
- Kovess-Masfety, V., Keyes, K., Hamilton, A., Hanson, G., Bitfoi, A., Golitz, D., Koc, C., Kuijpers, R., Lesinskiene, S., Mihova, Z., Otten, R., Fermanian, C., Pez, O., 2016. Is time spent playing video games associated with mental health, cognitive and social skills in young children? *Soc. Psychiatry Psychiatr. Epidemiol.* 51, 349–357.
- Lanningham-Foster, L., Jensen, T.B., Foster, R.C., Redmond, A.B., Walker, B.A., Heinz, D., Levine, J.A., 2006. Energy expenditure of sedentary screen time compared with active screen time for children. *Pediatrics* 118, e1831–1835.
- Lau, H.M., Smit, J.H., Fleming, T.M., Ripper, H., 2017. Serious games for mental health: are they accessible, feasible, and effective? A systematic review and meta-analysis. *Front. Psychiatry* 7, 209.
- Law, M., King, G., King, S., Kertoy, M., Hurley, P., Rosenbaum, P., Young, N., Hanna, S., 2006. Patterns of participation in recreational and leisure activities among children with complex physical disabilities. *Dev. Med. Child Neurol.* 48, 337–342.
- Lester, S., Russel, W., 2008. *Play for a change. Play, Policy and Practice: a Review of Contemporary Perspectives*, by Play England. <http://www.playengland.org.uk/resources-list>.
- Lillard, A.S., 2017. Why do the children (Pretend) play? *Trends Cogn. Sci. (Regul. Ed.)* 21, 826–834.
- Limperg, P.F., Peters, M., Colland, V.T., van Ommen, C.H., Beijleveld, M., Grootenhuys, M.A., Haverman, L., 2015. Reliability, validity and evaluation of the haemophilia coping and perception test. *Haemophilia* 21, e243–246.
- Lobel, A., Granic, I., Engels, R.C.M.E., 2014. Stressful gaming, interoceptive awareness, and emotion regulation tendencies: a novel approach. *Cyberpsychol. Behav. Soc. Netw.* 17, 222–227.
- Lum, A., Wakefield, C.E., Donnan, B., Burns, M.A., Fardell, J.E., Marshall, G.M., 2017. Understanding the school experiences of children and adolescents with serious chronic illness: a systematic meta-review. *Child Care Health Dev.* 43, 645–662.
- Maes, M., Van den Noortgate, W., Fustolo-Gunnink, S.F., Rassart, J., Luyckx, K., Goossens, L., 2017. Loneliness in children and adolescents with chronic physical conditions: a meta-analysis. *J. Pediatr. Psychol.* 42, 622–635.
- McAdams, D.P., 1995. What do we know when we know a person? *J. Pers.* 63, 365–396.
- McGonigal, J., 2011. *Reality Is Broken: Why Games Make Us Better and How They Can Change the World*. McGraw-Hill, New York.
- McLean, K.C., 2005. Late adolescent identity development: narrative meaning making and memory telling. *Dev. Psychol.* 41, 683–691.
- Merry, S.N., Stasiak, K., Shepherd, M., Frampton, C., Fleming, T., Lucassen, M.F., 2012. The effectiveness of SPARX, a computerised self help intervention for adolescents seeking help for depression: randomised controlled non-inferiority trial. *BMJ* 344 e2598.
- Møller, P., Husby, R., 2000. The initial prodrome in schizophrenia: searching for naturalistic core dimensions of experience and behavior. *Schizophr. Bull.* 26, 217–232.
- Mokkink, L.B., van der Lee, J.H., Grootenhuys, M.A., Offringa, M., Heymans, H.S., Dutch National Consensus Committee Chronic Diseases, Health Conditions in Childhood, 2008. Defining chronic diseases and health conditions in childhood (0–18 years of age): national consensus in the Netherlands. *Eur. J. Pediatr.* 167, 1441–1447.
- Moore, E.R., Bennett, K.L., Dietrich, M.S., Wells, N., 2015. The effect of directed medical play on young children's pain and distress during burn wound care. *J. Pediatr. Health Care* 29, 265–273.
- Moreno Cellieri, A.M., Poppe, R.W., 2016. Automatic behavior analysis in tag games: from traditional spaces to interactive playgrounds. *J. Multimodal User Interfaces* 10, 63–75.
- Murray, C.J., Richards, M.A., Newton, J.N., Fenton, K.A., Anderson, H.R., Atkinson, C., Bennett, D., Bernabe, E., Blencowe, H., Bourne, R., Braithwaite, T., Brayne, C., Bruce, N.G., Brughha, T.S., Burney, P., Dherani, M., Dolk, H., Edmond, K., Ezzati, M., Flaxman, A.D., Fleming, T.D., Freedman, G., Gunnell, D., Hay, R.J., Hutchings, S.J., Ohno, S.L., Lozano, R., Lyons, R.A., Marcenes, W., Naghavi, M., Newton, C.R., Pearce, N., Pope, D., Rushton, L., Salomon, J.A., Shibuya, K., Vos, T., Wang, H., Williams, H.C., Woolf, A.D., Lopez, A.D., Davis, A., 2013. UK health performance: findings of the Global Burden of Disease Study 2010. *Lancet* 381, 997–1020.
- Naber, F.B., Bakermans-Kranenburg, M.J., van IJzendoorn, M.H., Swinkels, S.H., Buitelaar, J.K., Dietz, C., van Daalen, E., van Engeland, H., 2008. Play behavior and attachment in toddlers with autism. *J. Autism Dev. Disord.* 38, 857–866.
- National Institute for Play, 2018. <http://www.nifplay.org/>.
- Nijhof, L.N., van de Putte, E.M., Wulfraat, N.M., Nijhof, S.L., 2016. Prevalence of severe fatigue among adolescents with pediatric rheumatic diseases. *Arthritis Care Res. (Hoboken)* 68, 108–114.
- Northman, L., Ross, S., Morris, M., Tarquini, S., 2015. Supporting pediatric cancer survivors with neurocognitive late effects: a model of care. *J. Pediatr. Oncol. Nurs.* 32, 134–142.
- Noyes, J., 2006. Health and quality of life of ventilator-dependent children. *J. Adv. Nurs.* 56, 392–403.
- Olzowski, A.E., Wolbrink, T.A., 2017. Serious gaming in medical education: a proposed structured framework for game development. *Simul. Healthc.* 12, 240–253.
- Panksepp, J., Sivi, S.M., Normansell, L., 1984. The psychobiology of play: theoretical and methodological perspectives. *Neurosci. Biobehav. Rev.* 8, 465–492.
- Patel, A., Schieble, T., Davidson, M., Tran, M.C., Schoenberg, C., Delphin, E., Bennett, H., 2006. Distraction with a hand-held video game reduces pediatric preoperative anxiety. *Paediatr. Anaesth.* 16, 1019–1027.
- Patenaude, A.F., Kupst, M.J., 2005. Psychosocial functioning in pediatric cancer. *J. Pediatr. Psychol.* 30, 9–27.
- Peckham, V.C., 1991. Learning disabilities in long-term survivors of childhood cancer: concerns for parents and teachers. *Int. Disabil. Stud.* 13, 141–145.
- Pellegrini, A.D., Smith, P.K., 1998. The development of play during childhood: forms and

- possible functions. *Child Psychol. Psychiatry Rev.* 3, 51–57.
- Pellis, S.M., 1988. Agonistic versus amicable targets of attack and defense: consequences for the origin, function and descriptive classification of play-fighting. *Aggr. Behav.* 14, 85–104.
- Pellis, S.M., Pellis, V.C., 2005. Play and fighting. In: Whishaw, I.Q., Kolb, B. (Eds.), *The Behavior of the Laboratory Rat: A Handbook With Tests*. Oxford University Press, Oxford, UK, pp. 298–306.
- Pellis, S.M., Pellis, V.C., 2009. *The Playful Brain: Venturing to the Limits of Neuroscience*. Oxford: Oneworld.
- Pellis, S.M., Pellis, V.C., 2017. What is play fighting and what is it good for? *Learn. Behav.* 45, 355–366.
- Pellis, S.M., Field, E.F., Smith, L.K., Pellis, V.C., 1997. Multiple differences in the play fighting of male and female rats. Implications for the causes and functions of play. *Neurosci. Biobehav. Rev.* 21, 105–120.
- Pendley, J.S., Dahlquist, L.M., Dreyer, Z., 1997. Body image and psychosocial adjustment in adolescent cancer survivors. *J. Pediatr. Psychol.* 22, 29–43.
- Perrin, J.M., Bloom, S.R., Gortmaker, S.L., 2007. The increase of childhood chronic conditions in the United States. *JAMA* 297, 2755–2759.
- Phillips, J., 2003. Psychopathology and the narrative self. *Philos. Psychiatr. Psychol.* 10, 313–328.
- Piaget, J., 1962. *Play, Dreams and Imitation in Childhood*. W.W. Norton & Company Inc, New York.
- Pinquart, M., 2017. Systematic review: bullying involvement of children with and without chronic physical illness and/or physical/sensory disability—a meta-analytic comparison with healthy/non-disabled peers. *J. Pediatr. Psychol.* 42, 245–259.
- Pinquart, M., Shen, Y., 2011. Behavior problems in children and adolescents with chronic physical illness: a meta-analysis. *J. Pediatr. Psychol.* 36, 1003–1016.
- Pinquart, M., Teubert, D., 2012. Academic, physical, and social functioning of children and adolescents with chronic physical illness: a meta-analysis. *J. Pediatr. Psychol.* 37, 376–389.
- Plechawska-Wójcik, M., Jakub, G., 2015. Implementation of serious game techniques in raising the social awareness of the depression disease. ICERI Conference Proceedings.
- Poder, U., Ljungman, G., von Essen, L., 2008. Posttraumatic stress disorder among parents of children on cancer treatment: a longitudinal study. *Psychooncology* 17, 430–437.
- Poppelaars, M., Tak, Y.R., Lichtwarck-Aschoff, A., Engels, R.C., Lobel, A., Merry, S.N., Lucassen, M.F., Granic, I., 2016. A randomized controlled trial comparing two cognitive-behavioral programs for adolescent girls with subclinical depression: a school-based program (Op Volle Kracht) and a computerized program (SPARX). *Behav. Res. Ther.* 80, 33–42.
- Potas, C., De Varela, M.J., De Carvalho, L.C., Do Prado, L.F., Do Prado, G.F., 2013. Effect of play activities on hospitalized children's stress: a randomized clinical trial. *Scand. J. Occup. Ther.* 20, 71–79.
- Redd, W.H., Jacobsen, P.B., Die-Trill, M., Dermatis, H., McEvoy, M., Holland, J.C., 1987. Cognitive/attentional distraction in the control of conditioned nausea in pediatric cancer patients receiving chemotherapy. *J. Consult. Clin. Psychol.* 55, 391–395.
- Rideout, V.J., Foher, U.G., Roberts, D.F., 2010. *Generation M2: Media in the Lives of 8-18-Year-Olds*. A Kaiser Family Foundation Study. <http://www.kff.org/entmedia/8010.cfm>.
- Rolland, J.S., Walsh, F., 2006. Facilitating family resilience with childhood illness and disability. *Curr. Opin. Pediatr.* 18, 527–538.
- Russoniello, C.V., O'Brien, K., Parks, J.M., 2009. The effectiveness of casual video games in improving mood and decreasing stress. *J. Cyber Ther. Rehabil.* 2, 53–66.
- Ryan, R.M., Rigby, C.S., Przybylski, A., 2006. The motivational pull of video games: a self-determination theory approach. *Motiv. Emot.* 30, 347–363.
- Schneider, P., Hannusch, C., Schmahl, C., Bohus, M., Spanagel, R., Schneider, M., 2014. Adolescent peer-rejection persistently alters pain perception and CB1 receptor expression in female rats. *Eur. Neuropsychopharmacol.* 24, 290–301.
- Schneider, P., Bindila, L., Schmahl, C., Bohus, M., Meyer-Lindenberg, A., Lutz, B., Spanagel, R., Schneider, M., 2016. Adverse social experiences in adolescent rats result in enduring effects on social competence, pain sensitivity and endocannabinoid signaling. *Front. Behav. Neurosci.* 10, 203.
- Scholten, H., Malmberg, M., Lobel, A., Engels, R.C., Granic, I., 2016. A randomized controlled trial to test the effectiveness of an immersive 3D video game for anxiety prevention among adolescents. *PLoS One* 11, e0147763.
- Schoneveld, E.A., Malmberg, M., Lichtwarck-Aschoff, A., Verheijen, G.P., Engels, R.C.M.E., Granic, I., 2016. A neurofeedback video game (MindLight) to prevent anxiety in children: a randomized controlled trial. *Comput. Hum. Behav.* 63, 321–333.
- Schuurmans, A.A., Nijhof, K.S., Vermaes, I.P., Engels, R.C., Granic, I., 2015. A pilot study evaluating "Dojo," a videogame intervention for youths with externalizing and anxiety problems. *Games Health J.* 4, 401–408.
- Seligman, M.E.P., 2002. Positive psychology, positive prevention, and positive therapy. *Handbook of Positive Psychology* (2002). Oxford: Oxford University Press. Handbook of positive psychology. Oxford University Press, Oxford, pp. 3–9.
- Shields, L., 2001. A review of the literature from developed and developing countries relating to the effects of hospitalization on children and parents. *Int. Nurs. Rev.* 48, 29–37.
- Siviy, S.M., Harrison, K.A., 2008. Effects of neonatal handling on play behavior and fear towards a predator odor in juvenile rats (*Rattus norvegicus*). *J. Compar. Psychol.* (Washington, D.C.): 122, 1–8.
- Siviy, S.M., Panksepp, J., 1985. Energy balance and play in juvenile rats. *Physiol. Behav.* 35, 435–441.
- Siviy, S.M., Harrison, K.A., McGregor, I.S., 2006. Fear, risk assessment, and playfulness in the juvenile rat. *Behav. Neurosci.* 120, 49–59.
- Siviy, S.M., Steets, C.L., DeBrouse, L.M., 2010. Effects of chlordiazepoxide on predator odor-induced reductions of playfulness in juvenile rats. *Behav. Brain Res.* 206, 254–262.
- Smilansky, S., Shefatya, L., 1990. *Facilitating Play: A Medium for Promoting Cognitive, Socio-Emotional and Academic Development in Young Children*. Psychological & Educational Publications.
- Špinka, M., Newberry, R.C., Bekoff, M., 2001. Mammalian play: training for the unexpected. *Q. Rev. Biol.* 76, 141–168.
- Spirito, A., Stark, L.J., Cobiella, C., Drigan, R., Androkites, A., Hewett, K., 1990. Social adjustment of children successfully treated for cancer. *J. Pediatr. Psychol.* 15, 359–371.
- Stam, H., Grootenhuys, M.A., Last, B.F., 2005. The course of life of survivors of childhood cancer. *Psychooncology* 14, 227–238.
- Stam, H., Hartman, E.E., Deurloo, J.A., Groothoff, J., Grootenhuys, M.A., 2006. Young adult patients with a history of pediatric disease: impact on course of life and transition into adulthood. *J. Adolesc. Health* 39, 4–13.
- Sutton-Smith, B., 2008. Play theory - a personal journey of new thoughts. *Am. J. Play* 1, 80–123.
- Takhvar, M., Smith, P.K., 1990. A review and critique of Smilansky's classification scheme and the "nested hierarchy" of play categories. *J. Res. Child. Educ.* 4, 112–122.
- Tate, R., Haritatos, J., Cole, S., 2009. HopeLab's approach to re-mission. *Int. J. Learn. Media* 1, 29–35.
- Timko, C., Baumgartner, M., Moos, R.H., Miller 3rd, J.J., 1993. Parental risk and resistance factors among children with juvenile rheumatic disease: a four-year predictive study. *J. Behav. Med.* 16, 571–588.
- Trezza, V., Damsteegt, R., Vanderschuren, L.J.M.J., 2009. Conditioned place preference induced by social play behavior: parametrics, extinction, reinstatement and disruption by methylphenidate. *Eur. Neuropsychopharmacol.* 19, 659–669.
- Trezza, V., Campolongo, P., Vanderschuren, L.J.M.J., 2011. Evaluating the rewarding nature of social interactions in laboratory animals. *Dev. Cogn. Neurosci.* 1, 444–458.
- UMCU and WKZ sportief. <http://www.hetwvz.nl/nl/Ziekenhuis/Afdelingen/Kinderbewegingscentrum/WKZ-Sportief/WKZ-Sportief-Op-Weg>.
- Ungerer, J.A., Sigman, M., 1981. Symbolic play and language comprehension in autistic children. *J. Am. Acad. Child Psychiatry* 20, 318–337.
- Uttal, D.H., Meadow, N.G., Tipton, E., Hand, L.L., Alden, A.R., Warren, C., Newcombe, N.S., 2013. The malleability of spatial skills: a meta-analysis of training studies. *Psychol. Bull.* 139, 352–402.
- Van Berckelaer-Onnes, I.A., 2003. Promoting early play. *Autism* 7, 415–423.
- van Brussel, M., van der Net, J., Hulzebos, E., Helden, P.J., Takken, T., 2011. The Utrecht approach to exercise in chronic childhood conditions: the decade in review. *Pediatr. Phys. Ther.* 23, 2–14.
- Van Cleave, J., Gortmaker, S.L., Perrin, J.M., 2010. Dynamics of obesity and chronic health conditions among children and youth. *JAMA* 303, 623–630.
- van den Berg, C.L., Hol, T., Van Ree, J.M., Spruijt, B.M., Everts, H., Koolhaas, J.M., 1999. Play is indispensable for an adequate development of coping with social challenges in the rat. *Dev. Psychobiol.* 34, 129–138.
- Van der Geest, K.E., Merelle, S.Y.M., Rodenburg, G., Van de Mheen, D., Renders, C.M., 2017. Cross-sectional associations between maternal parenting styles, physical activity and screen sedentary time in children. *BMC Public Health* 17, 753.
- van Gils, A., Janssens, K.A., Rosmalen, J.G., 2014. Family disruption increases functional somatic symptoms in late adolescence: the TRAILS study. *Health Psychology: Official Journal of the Division of Health Psychology Vol 33*. American Psychological Association, pp. 1354–1361.
- van Rooij, M., Lobel, A., Harris, O., Smit, N., Granic, I., 2016. DEEP: a biofeedback virtual reality game for children at risk for anxiety. *Proceedings of the 2016 CHI Conference Extended Abstracts on Human Factors in Computing Systems 1989–1997*. <https://doi.org/10.1145/2851581.2892452>.
- Vanderschuren, L.J.M.J., Trezza, V., 2014. What the laboratory rat has taught us about social play behavior: role in behavioral development and neural mechanisms. *Curr. Top. Behav. Neurosci.* 16, 189–212.
- Vanderschuren, L.J.M.J., Niesink, R.J., Spruijt, B.M., Van Ree, J.M., 1995. Influence of environmental factors on social play behavior of juvenile rats. *Physiol. Behav.* 58, 119–123.
- Vanderschuren, L.J.M.J., Niesink, R.J., Van Ree, J.M., 1997. The neurobiology of social play behavior in rats. *Neurosci. Biobehav. Rev.* 21, 309–326.
- Vanderschuren, L.J.M.J., Achterberg, E.J., Trezza, V., 2016. The neurobiology of social play and its rewarding value in rats. *Neurosci. Biobehav. Rev.* 70, 86–105.
- Vannatta, K., Zeller, M., Noll, R.B., Koontz, K., 1998. Social functioning of children surviving bone marrow transplantation. *J. Pediatr. Psychol.* 23, 169–178.
- Vasterling, J., Jenkins, R.A., Tope, D.M., Burish, T.G., 1993. Cognitive distraction and relaxation training for the control of side effects due to cancer chemotherapy. *J. Behav. Med.* 16, 65–80.
- Vermaes, I.P., van Susante, A.M., van Bakel, H.J., 2012. Psychological functioning of siblings in families of children with chronic health conditions: a meta-analysis. *J. Pediatr. Psychol.* 37, 166–184.
- Von Frijtag, J.C., Schot, M., van den Bos, R., Spruijt, B.M., 2002. Individual housing during the play period results in changed responses to and consequences of a psychosocial stress situation in rats. *Dev. Psychobiol.* 41, 58–69.
- Wallander, J.L., Varni, J.W., 1998. Effects of pediatric chronic physical disorders on child and family adjustment. *J. Child Psychol. Psychiatry* 39, 29–46.
- Wiener, L., Battles, H., Mamalian, C., Zadeh, S., 2011. ShopTalk: a pilot study of the feasibility and utility of a therapeutic board game for youth living with cancer. *Support. Care Cancer* 19, 1049–1054.
- Wijnhoven, L.A., Creemers, D.H., Engels, R.C., Granic, I., 2015. The effect of the video game Mindlight on anxiety symptoms in children with an Autism Spectrum disorder. *BMC Psychiatry* 15, 138.
- Wise, P.H., 2007. The future pediatrician: the challenge of chronic illness. *J. Pediatr.* 151, S6–10.
- Wittgenstein, L., 1953. *Philosophical Investigations*. MacMillan Publishing Company.