

# Does the child brain rest?: An examination and interpretation of resting cognition in developmental cognitive neuroscience

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## ABSTRACT

In cognitive neuroscience, measurements of “resting baseline” are often considered stable across age and used as a reference point against which to judge cognitive state. The task-based approach—comparing resting baseline to task conditions—implies that resting baseline is an equalizer across participants and—in the case of studies of developmental changes in cognition—across age groups. In contrast, network neuroscience explicitly examines the development of “resting state” networks across age, at odds with the idea of a consistent resting baseline. Little attention has been paid to *how* cognition during rest may shift across development, particularly in children under the age of eight. Childhood is marked by striking maturation of neural systems, including a protracted developmental period for cognitive control systems. To grow and shape these cognitive systems, children have a developmental imperative to engage their neural circuitry at every possible opportunity. Thus, periods of “rest” without specific instructions may require additional control for children as they fight against developmental expectation to move, speak, or otherwise engage. We therefore theorize that the child brain does *not* rest in a manner consistent with the adult brain as longer rest periods may represent increased cognitive control. To shape this theory, we first review the extant literature on neurodevelopment across early childhood within the context of cognitive development. Next, we present nascent evidence for a destabilized baseline for comparisons across age. Finally, we present recommendations for designing, analyzing, and interpreting tasks conducted with young children as well as for resting state. Future work must aim to tease apart the cognitive context under which we examine functional brain development in young children and take considerations into account unique to each age.

## 1. Introduction: why question rest in the child brain?

Across the last decade, there has been an explosion of neuroscience studies investigating cognitive networks in the resting brain with relatively little attention being paid to how the cognitive processes engaged during rest itself may shift across development. Examinations of the neural signatures of rest include “resting state” (Biswal et al., 1995; Damoiseaux et al., 2006; Fox et al., 2005) measurements, in which a participant is instructed to simply rest and let their mind wander for several minutes, and short periods of “resting baseline” (Dale, 1999; Fair et al., 2007; Shan et al., 2014) in which a brief period of rest is inserted between task conditions—such as an inter-stimulus, -trial, or -block

interval rest period—to be measured as a neutral comparison to the neural state that the task provokes. A recent PubMed search of the general terms “Brain” and “Rest” from 2008 to 2018 revealed 9776 total publications (average of 889 per year) meeting these search criteria, representing a 109% increase from 2008 (498 publications) to 2018 (1039 publications). This stands in stark contrast to the five-year period immediately preceding the last decade in which a total of 1928 publications met this general search criteria, remaining relatively steady from 2003 (340 publications) to 2007 (415 publications; 22% increase).<sup>1</sup> As interest in the resting adult brain has intensified, and measurement methodology become more sophisticated, interest has grown for the examination of rest in studies of human brain development. Indeed,

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<sup>1</sup> We note that the period from 2017 (1288 publications) to 2018 (1039 publications) represented the only significant decrease in publications returned based on the search criteria across the last 20 years. While it is too early to determine whether the decrease during the last year represents a one-year deviation from the increasing pattern or whether a decreasing trend has begun, we offer that this decrease may represent a general questioning of the theoretical interpretation of rest across the field, as suggested within the current discussion.

several large-scale, national, multi-million-dollar studies (e.g. Adolescent Brain Cognitive Development Study-ABCD; Baby Connectome Project; Environmental Influences on Child Health Outcomes-ECHO) and publicly available data sets (e.g. Philadelphia Neurodevelopmental Cohort-PNC (Satterthwaite et al., 2016); Pediatric Imaging, Neurocognition, and Genetics Data Repository-PING (Jernigan et al., 2016)) include resting state scanning, with some data sets including task-based resting baseline. All of these data sets examine the resting brain before the age of 18, many repeating resting fMRI scans longitudinally in order to assess maturational changes across development. Resting state data collection might be particularly amenable to data gathering in large multi-site studies due to relative uniformity in administration, ability for children across age to understand task instructions, and potential for comparison with outside studies and with the scientific literature. While it seems, however, that resting state data collection has become a somewhat unspoken requirement within developmental cognitive neuroscience studies in order to examine changes in cognitive networks across time, resting baseline is already ubiquitous during tasks and is often reported in a manner seemingly at odds with the cognitive network development literature. In other words, little attention has been paid to the conjunction of these two approaches—does a child truly rest comparably across development during resting baselines in task if the networks that support that cognition are still developing? That is, it is still unexplored whether the child brain rests to the same degree as that of an adult brain, whether what we describe as rest represents a different cognitive process for children entirely, or how that degree of change or shifting of the process might mature across development.

Indeed, resting baseline in child samples has often been considered an “equalizer”, such that a condition of interest that is expected to change across age is examined in comparison to a rest condition that is conceptualized to be equal across all subjects. In other words, the way in which task-based data is analyzed—a condition modeled against baseline activity either explicitly or implicitly—assumes that resting baseline represents a consistent cognitive state across groups and ages even though researchers often ignore resting cognition when designing and interpreting their analyses. There is a growing body of work to suggest that resting cognition during resting baselines are related to context-specific cognition, even in adults. For example, studies investigating prefrontal and parietal development underlying working memory often introduce a spatial or verbal working memory condition compared to a resting baseline. Results have demonstrated increased frontal and parietal activation and integration as the brain matures, which has been attributed to increased executive function abilities (Buss et al., 2014; Geier et al., 2009; Kwon et al., 2002; Perlman et al., 2016; Scherf et al., 2006). What has not been considered, however, is that the rest condition might also be changing as children become “better resters.” In other words, it is likely that the cognitive ability to relax top-down cognitive control and allow one’s mind to wander changes with the development of the underlying neural networks that support this cognitive ability to rest. As children improve in the ease with which they can remain still and can engage in a lower-order cognitive state during the rest period, there may be greater observed activation differences when comparing conditions of interest to longer periods of resting baseline. In contrast, short inter-trial or inter-stimulus intervals (i.e., short periods of resting baseline) likely differ in adults and children for another reason—adults are likely engaging in preparatory cognition while young children are likely not as prepared. The possibility that resting baseline is associated with distinct cognitive states in children and adults (and that this state varies by context) is important to consider given evidence that greater activation of the default mode network (DMN; Buckner et al., 2008; Greicius et al., 2003), which engages when the brain is not absorbed in task, during these short resting baseline periods predicts enhanced integration of regions involved in working memory and better performance during a working memory task (Alavash et al., 2015; Hampson et al., 2006; Newton et al., 2011; Sala-Llanch et al., 2012). It has even been

demonstrated that working memory training can lead to increased functional connectivity within the fronto-parietal network (FPN), the network most involved in executive function, which also correlates with increased working memory performance, and decreased DMN activation during a resting period before a working memory task (Jolles et al., 2013). This indicates that greater working memory skill engages preparatory mechanisms in the moments before the appropriate neural circuitry is needed to activate, even during periods in which a subject is technically at rest, suggesting that rest can also serve as a preparatory period for the brain. It is highly unlikely that young children engage in preparatory cognition to a similar degree as adults considering that children are still developing their higher level cognitive skills well into adolescence (Anderson, 2002; Luna et al., 2004; Luna et al., 2010). Though investigations of the resting state networks in relation to working memory abilities in children are sparse, one multi-modal study using fMRI and magnetoencephalography (MEG) found that greater functional connectivity within the fronto-parietal network, at rest, predicted enhanced working memory abilities (Barnes et al., 2016). Thus, the possibility that rest itself is a dynamic process, changing across age, is especially important to consider given evidence of changes in resting state connectivity across both task positive networks and neural coordination of networks activated during rest.

We propose that in light of the increasing evidence of the brain’s maturation during rest over the past decade, that the time has arrived for the field to carefully consider the theoretical implications of the assumption of rest as an equalizer. The methodological issues associated with attributing change in one condition (“Task A”) to what may actually be an unnoticed difference in a comparison (“Task B”) between groups has been discussed before (Church et al., 2010). The “Task B” issue highlights the problematic comparison of subtracted task conditions between age groups when task demands are not actually equal across ages (i.e., the within subject subtraction of Task A minus Task B represents a different cognitive comparison in children compared to adults). We argue, however, that rest is a deviation from the so-called “Task B Problem” in that 1) rest is often not considered as a task, and, therefore, overlooked as a changing cognitive state across development and 2) resting activity does not represent a consistent cognitive state across development from infancy to adulthood, but represents an entirely different process at young ages. Recent work has elucidated a richer neurodevelopmental context in which to explore and understand rest as a changing baseline, particularly in children under 8. Thus, we seek to reexamine these issues in the context of infancy through adolescence, discuss the nature of rest within the context of human development from both the cognitive and neural perspectives, and provide recommendations for studying cognitive neurodevelopment in young populations. Our overall goal is therefore to explore the possibility that rest is not a consistent construct across development, as is generally assumed, but instead changes in behavioral and brain function over time. We note that the intention of this analysis is not to disqualify rest as a valid condition for neuroscientific studies, but to turn a critical eye towards the meaning of rest, in order to better interpret its scientific value within a developmental framework. Thus, we posit that research in development, particularly within the early periods, must reexamine how we analyze and interpret our work to account for a changing baseline. This is particularly timely as several of the multi-site, national, pediatric neuroimaging studies described above are anticipating their first data releases and new “big data” projects including resting methodology are being formed. Briefly, we also note that the considerations presented here can be applied beyond the study of healthy cognitive development. There are many illnesses that can incur deviations from the typical experience of “rest”—such as chronic pain (Baliki et al., 2011; Malinen et al., 2010) or psychiatric disorders such as attention deficit hyperactivity disorder (ADHD; Hoekzema et al., 2014; Yu-Feng et al., 2007) — which can also benefit from careful consideration of what “rest” means when studying these populations.

## 2. Examining the resting brain across development

### 2.1. The biological basis of resting state activity in the mature brain

While the true underlying neurobiology that gives rise to resting state cognitive networks have yet to be fully elucidated, emerging work in adults, combined with invasive work conducted in animals, provide a window into the potential neurobiological mechanisms in youth. It is theorized that the resting temporal dynamics of this neural activity may be a mixture of representations of preparatory cognition (i.e., predicting the next needed action or the next observed stimuli) (Alavash et al., 2015; Hampson et al., 2006; Jolles et al., 2013; Sala-Llonch et al., 2012), signal associated with mind-wandering and other inward-directed cognition (Buckner and DiNicola, 2019; Christoff et al., 2009), and shared physiological noise among other sources. The spontaneous activity that underlies this cognition is critical for general cognitive functioning (Raichle, 2010). There is evidence in the context of plasticity research to support this theory across domains of neuroscience work—from invasive neuronal recordings to human fMRI—that demonstrates that resting neural activity and neural structure is modifiable via learning (Doyon and Benali, 2005; Jolles et al., 2013; Lendvai et al., 2000; Lewis et al., 2009; Rebola et al., 2010; Ungerleider et al., 2002). Further, resting cognition changes dramatically as a result of injury such as epilepsy or traumatic brain injury and is shown to be restored with successful treatment (Gilbert et al., 2018; Pizoli et al., 2011). In the context of resting state fMRI and fNIRS, another important source of resting signal comes from slow (<0.1 Hz) changes in arteriole vasomotion, which is entrained by neuronal activity in the gamma band (Mateo et al., 2017). Taken together, this evidence suggests that spontaneous resting neuronal signals are a result of long-term learning and are critical for both internally and externally motivated cognition as well as general functioning. Importantly for fMRI and fNIRS measurement, the neuronal plasticity that underlies resting signal also entrains the local blood flow in harmonized hemodynamics.

### 2.2. The anatomical and physiological demands of brain development

Childhood is marked by profound and often nonlinear changes in the brain that support large gains in all aspects of behavioral and cognitive functioning. There is evidence that the number of synapses formed per neuron across the cortex peaks at non-uniform points between the ages of 3–8 and remains relatively stable across childhood thereafter (Huttenlocher, 1990; Huttenlocher et al., 1982; Petanjek et al., 2011). In large, in vivo, longitudinal studies of human cortex development from age 4 through adulthood, cortical thickness peaks during early to late childhood for most brain regions, with the prefrontal and insular cortex peaking the latest at approximately 14–17 years of age (Raznahan et al., 2011a; Raznahan et al., 2011b; Raznahan et al., 2014; Shaw et al., 2008; Tamnes et al., 2017). Though longitudinal structural neuroimaging studies across early childhood are scarce, studies that include children under five years-old show that the largest relative increases in cortical thickness are made before the age of 3 with a slight slowing of growth through age 6 (Knickmeyer et al., 2008; Shaw et al., 2008). The steady increase in cortical thickness between ages 2 and 6 is primarily due to increased dendritic branching—likely of Layer III pyramidal neurons (Petanjek et al., 2019)—accompanied by cortical myelination of these connections (Deoni et al., 2011; Remer et al., 2017). Work in resting EEG suggest that these synaptic changes support the neural oscillations that shift throughout development. Specifically, there is evidence that resting delta and theta power decreases with age while alpha, gamma, and beta increase with cortical maturation (Chiang et al., 2011; Clarke et al., 2001; Penuel et al., 1955; Segalowitz et al., 2010). In other words, slow oscillations in neuronal firing are gradually replaced with faster oscillations as the cortex develops in a spatial pattern consistent with the maturational pattern of the cortex, with posterior and parietal areas shifting faster than anterior prefrontal regions. The synaptogenesis in early childhood and

synaptic pruning in late childhood and adolescence therefore likely underlie these shifting large scale firing patterns in the cortex (see also Buchmann et al., 2011) and higher level cognitive development (Koenig et al., 2002; Vakorin et al., 2011; Vakorin et al., 2013). This complex, coordinated, and non-uniform development of the brain during early childhood forms the basis for behavior and cognition and is, therefore, an initial clue that any cognitive state is in flux during childhood as these foundational circuits are formed.

Rich neurovasculature development supports the foundational neuronal maturation in early childhood giving rise to the coordinated neuronal-hemodynamic response. This is an important point to consider given that a large portion of human cognitive neuroscience work is conducted using methods that indirectly measure local neuronal firing via shifts in local blood flow—such as fMRI (blood oxygen level dependent signal or BOLD) and fNIRS (oxygenated hemoglobin or HbO). Interpretation of the hemodynamic response is based on studies that identify coupling between neuronal population firing and an initial increase in de-oxygenated hemoglobin (Hb) followed by a striking increase in HbO-rich blood flow to the area, resulting in decreased concentration of Hb relative to HbO (Arthurs and Boniface, 2002; Hillman, 2014; Logothetis et al., 2001). It is unclear at what age the stereotyped neuronal hemodynamic response emerges, however. Indeed, human task-based fMRI and fNIRS studies have identified a mixture of positive, negative, and delayed hemodynamic responses to environmental stimuli in children under 5 (Arichi et al., 2012, 2010; Born et al., 2000; Deen et al., 2017; Issard and Gervain, 2018; Meek et al., 1998; Minagawa-Kawai et al., 2011; Yamada et al., 1997). Recent work using rat models indicates that neuronal-hemodynamic coupling is not well established until rats are past postnatal day 23 (Kozberg et al., 2013; Kozberg and Hillman, 2016), which corresponds to the point at which neurovasculature reaches adult-like length and branching (Harb et al., 2013). It is difficult to make an exact comparison between rodent and human developmental stages as rodents lack a childhood period. Based on weaning behaviors in rats and human EEG neuronal firing development, postnatal day 23 likely corresponds to some point during the toddler years (Marshall et al., 2002; Penuel et al., 1955; Sengupta, 2013). Task and non-task activation that is measured indirectly via measurements of blood flow is therefore not likely stabilized in much of early childhood—specifically during the infancy and toddler years—while the neuronal-hemodynamic relationship is still emerging and refining. In other words, as will be explored more in Section 3, both explicit and implicit resting baselines do not represent the same neurobiological processes between age groups (i.e., decreased BOLD in infants may be more akin to increased BOLD in adults for some cognitive processes).

What is happening neurally during “rest” in young children? One possibility that is raised in the animal literature is spontaneous activity. A long line of research has reliably found that spontaneous activity is not only a main driver of neuronal development but is *necessary* for development (Cang et al., 2005; Demas et al., 2003; Katz and Shatz, 1996; Lippe, 1994). While spontaneous activity-driven development does not require external input for foundational growth to take place in some systems (Demas et al., 2003), external experience is critically important once the foundations of the circuit are in place by the end of infancy (Khazipov and Luhmann, 2006). Thus, taking all the presented evidence together, we hypothesize that widespread networks of neurons fluctuate their activity at rest as children mature to propel this foundational development of the brain. As children experience the world, these neuronal populations develop shared firing histories and increasingly synchronized activity; the theoretical source of resting state networks (Raichle, 2010). Considering the rapid foundational development occurring across childhood, there is reason to expect that the same plasticity processes that link learning to changes in neural structure and function—i.e., neuronal activity driving structural and functional changes—are unfolding at a much more widespread and rapid rate in young children. This theory implies that young children likely have a much higher baseline rate of random neuronal activity in order to spur

this necessary foundational development. This heightened activity is likely spatially and temporally non-uniform, potentially contributing to the additional variance in neural signals observed in children compared to adults (Adleman et al., 2002; Kharitonova et al., 2015; Tsujimoto et al., 2004). Further, this heightened activity is likely indicative of dynamic, spontaneous cognition within the child that is aimed at developing the systems the child requires when the brain is not otherwise engaged in behavior. This aligns with the oft noted experience that children unengaged in meaningful task will spontaneously engage in motor or verbal activity, which decreases starting at around age 9 or 10 (Diessel and Tomasello, 2001; Kowal et al., 1975; von Hofsten, 2004), coinciding with just after the brain peaks in size. It is, therefore, likely that a young child's primary developmental directive to always be behaving in order to build the necessary foundational neural connections.

We raise the possibility that rest—and subsequently resting state or resting baseline measurement—is not indicative of simply a disengagement of outward activity or engagement of inward thought, as is often assumed, but instead represents an engaged cognitive state driven by developmental demand. When this corpus of neurobiological work is considered together, it becomes clear that children are not likely mind-wandering, even when instructed to do so, as is the case with most resting state fMRI work (Diessel and Tomasello, 2001; Greene et al., 2018; Kowal et al., 1975; Vanderwal et al., 2015; von Hofsten, 2004). Instead, we theorize that children exert significant cognitive effort to override their developmental demand to grow circuitry to support all aspects of behavior in order to comply with the demands of rest. Rest cannot, therefore, be considered an equalizer between age groups as changes in network activity across age are likely indicative of both cognitive development and cognitive emergence. That is, in the absence of adult-like spatial patterns of neural activation, it is difficult to know if individual differences in neural activation are due to neurodevelopmental differences or to differences in online cognitive demands.

### 2.3. Cognitive and neurobiological convergence in default mode and fronto-parietal network development

One means of examining the emergence of the ability to “rest” is by examining the network development that is thought to underlie this cognitive function. In mature adult brains, the networks most often studied in the context of baseline and resting state cognition are the fronto-parietal network (FPN) and default mode network (DMN). Each of these networks are diverse and likely composed of overlapping networks with nuanced functions (e.g., “mentalizing” versus “autobiographical memory recall” as reviewed in Buckner and DiNicola, 2019). For the purposes of this review, however, we generalize these more granular and overlapping networks to either FPN—denoting networks that direct externally-guided cognition—or DMN—denoting networks that underlie internally-focused cognition. From work with adults, there is evidence of a nuanced and dynamic relationship between these two networks during both task-engaged and resting periods. Specifically, there is evidence that widespread regions of the FPN are among the most globally connected in the brain (Cole et al., 2010; Power et al., 2011) and that the FPN may serve as a hub for organizing behavior (Cole et al., 2013). For a thorough discussion of this topic, see Marek and Dosenbach (2018).

Starting in infancy, the emerging spatial structure associated with resting state networks develop at an uneven and protracted rate concurrent to each network's associated cognitive development. The DMN decreases in activation during typical cognitive task performance while the FPN increases in activation (Binder et al., 1999; Gusnard and Raichle, 2001; Shulman et al., 1997; Thomason et al., 2008). In adults, adolescents, and older children, the DMN has been found to support introspective and social cognition (Gusnard et al., 2001; Richardson, 2018; Schilbach et al., 2008; Uddin et al., 2007). It is likely that the developmental trajectories of the DMN and FPN across childhood can elucidate the stages at which they may support cognition similar to that observed in adults. Several studies note that there is striking maturation of these

networks across childhood and adolescence with increasing modularity (Baum et al., 2017; Fair et al., 2008; Marusak et al., 2017; Power et al., 2010; Uddin et al., 2011) along with emerging anti-correlation between the two networks seen in children as young as one year (Gao et al., 2013). It is possible that, in young rapidly developing children, developmental demands may overshadow a drive to purely think introspectively when instructed to or by default in the absence of external stimuli. As is explored more thoroughly in Section 3, children show a wider range of neural activation (Adleman et al., 2002; Kharitonova et al., 2015; Tsujimoto et al., 2004) and increased physical movement (Greene et al., 2018; Vanderwal et al., 2018) both at resting baseline and during task conditions than do adults, particularly at younger ages, demonstrating a destabilized baseline in children compared to adults. The coordinated development of the DMN and the FPN is likely underlying this shift from wide variability across children to more narrow variability within adults. While there is evidence that subject motion inflates the age-related effects found in functional connectivity studies (Power et al., 2012; Satterthwaite et al., 2012; Van Dijk et al., 2012), work in older children and adolescents has found these effects to still be present even after rigorous motion correction (Satterthwaite et al., 2013).

There is evidence from seed-based resting state fMRI analysis that the architecture of the DMN is present in a basic form in infants as young as 6 months when coactivation of the bilateral inferior parietal lobule (IPL), posterior cingulate cortex (PCC), and medial prefrontal cortex (MPFC) comes online (Gao et al., 2015a,b). Using more data-driven approaches, however, the DMN does not distinguish itself from other brain network modules until past age one (Wen et al., 2019) with both DMN and non-DMN regions forming networks together in 1- and 2-year-olds (Gao et al., 2009). Thus, by the end of infancy, the regions that will eventually become the DMN are still integrating across the medial prefrontal and lateral parietal cortices to form a distinct network. To illustrate, Richardson (2018) reported that 3–12 year old children show a drastic increase in intra-network connectivity with age in DMN regions supporting social cognition, with clear network segregation starting at around age seven (Richardson et al., 2018). This pattern is likely a result of dramatic increases in local connectivity across DMN regions during the preschool years (Long et al., 2017). Further, several studies comparing 7–12 year old children to adolescents and adults show that DMN intra-network connectivity and network modularity increases dramatically across childhood to produce stable network architecture that is consistent across adolescence and adulthood (Fair et al., 2008, 2009; Marek et al., 2015; Supekar et al., 2010; Uddin et al., 2011). Taken together, this work provides a general timeline for DMN development: basic architecture builds across early and middle childhood while intra-network connectivity strengthens across adolescence, distinguishing it from other networks at the same time. This development is marked by high variability among still developing children compared to adults (Marusak et al., 2017; Supekar et al., 2010), evidence that DMN spatial structure and function are not equal across development.

The FPN, in contrast, has a more protracted and non-linear development of network architecture, intra-network connectivity, and inter-network dynamics. The adult architecture of the FPN typically includes the intraparietal sulcus (IPS) and dorsolateral prefrontal cortex (DLPFC) bilaterally. Regions of the dorsal cingulate, inferior temporal gyrus, and anterior insula are sometimes included in the network though not consistently, thus we focus on the DLPFC and IPS. It is as of yet unclear when the functional architecture of the FPN emerges in childhood, however, as resting state work with children during the preschool years is still scarce and both seed-based and network-based infants studies show that the frontal and parietal nodes of the network are not yet functionally integrated at age 2 (Gao et al., 2015a,b; Gao et al., 2011). In the only study of whole brain resting state connectivity in preschoolers, the intraparietal sulcal regions of the network increase in regional homogeneity and decrease in global connectivity across ages 2 through 6, though network membership of these regions was not explored (Long et al., 2017). Across late childhood and adolescence, the spatial structure



of the FPN varies both by developmental stage and by context. While the spatial topography of the FPN in relation to the DMN is relatively stable across late childhood and adolescence, there is evidence for increasing flexibility—transient coactivation with other networks—of the FPN in late adolescence and adulthood that corresponds to improvements in cognitive control (Marek et al., 2015; Medaglia et al., 2018). Further, as teens get older, their brains spend more and more time in a state reflecting clear coactivation of either DMN or FPN regions and less time in a mixed state (Medaglia et al., 2018), which may be indicative of the shifting network memberships of the IPS/IPL and precuneus across early and mid-adolescence (Marusak et al., 2017). This corpus of work highlights the unique development of the FPN with strong evidence that this network doesn't support the same cognition in children and young adolescents as it does with older teens and adults. In other words, the FPN has not fully established itself as a hub for organizing behavior in children and continues to develop in this role well into adolescence. Combined with what is known about DMN development, we posit that childhood “baseline” activity would include spontaneous activation of these fronto-parietal regions in order to drive development. This is at odds with the decreased activation of the FPN observed in adults during baseline measurements and is further evidence of a destabilized baseline in young children.

When we integrate these developmental trajectories, several considerations for interpreting baseline activation in children emerge: 1) there appears to be an inverse relationship between stability of “baseline” activity and age in childhood, 2) “baseline” DMN and FPN network topography does not evidence stability until late childhood, 3) integration of DMN and FPN networks is not achieved until mid to late adolescence, 4) coordinated activity of these cognitive networks supporting developed cognitive control is not achieved until late adolescence/early adulthood. These developmental trajectories are summarized in Fig. 1. This work suggests that young children are likely operating under vastly different cognitive and neurobiological conditions during tasks, and are nascent evidence of a destabilized baseline in childhood. An important issue to keep in mind, however, is that the vast majority of the works reviewed in this section do not adequately account for motion, physiological artifacts such as from cardiac pulse or respiration, or cognitive state from mixed methods that include having the child sleep, watch a movie, or fixate on a cross hair.

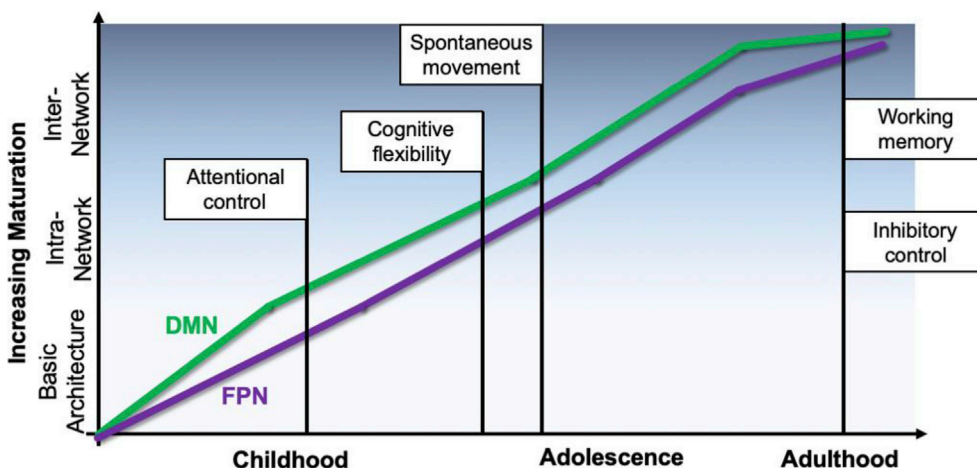


Fig. 1. Model of cognitive development focusing on the frontoparietal network and default mode network. The protracted development of these networks is divided into 3 phases for simplicity named for the type of network development that is largely and notably occurring at that stage. “Basic Architecture” refers to the spatial development of the functional network and is the most striking piece of neurodevelopment occurring in the first 3 years of life. “Intra-Network” refers to the sharp increase in within network connectivity that occurs across childhood as networks become more integrated. “Inter-network” refers to communication between networks, a developmental process that is refined across adolescence. Importantly, these stages of network are not confined to these age windows but occur to some degree across the lifespan. Checkpoints in cognitive development are denoted with black vertical lines indicating the approximate age at which children begin to perform these domains at adult levels. “Spontaneous movement” denotes the age at which movement during fMRI does not differ significantly between task and non-task contexts.

### 3. Comparing task to rest across childhood: unstable baselines and “deactivation” effects

There are several studies demonstrating a range of activation patterns that together indicate a destabilized baseline across early and middle childhood. More recent work has highlighted that across the lifespan resting state and resting baseline cognition are markedly different (Berchicci et al., 2015; Jonkman, 2006; Vatansever et al., 2015; Yan et al., 2009) and even that cognition during baseline conditions is predictive of performance during the task-positive conditions (De Blasio et al., 2013; Vatansever et al., 2015). This is likely due to a combination of factors. Critically, a baseline within a task is not generally a period of lower-order cognition, but rather a period of preparation for the next trial in the task. In children developing cognitive control, this implies that there is significant cognitive activity needed to perform both the baseline periods within a task and the task conditions. It is not surprising, then, that there are mixed patterns of activity in early and middle childhood neuroimaging work ranging from adult-like activation patterns to strikingly different results including negative task effects (i.e., more or equal activity during baseline compared to task activity) and inverted BOLD responses to stimuli. Thus, in this section we present evidence from task-based literature that—when taken together with the resting state and physiological changes occurring across early childhood—potentially indicate shifting baseline cognition across maturation.

#### 3.1. Task activation patterns in infants and toddlers are age and cognition-specific

Infant imaging studies demonstrate the interaction between developmental stage, cognition, and baseline activation across imaging modalities in nuanced ways. Studies of newborn infants have found an expected increased BOLD response in somatosensory cortex during arm movement but not during the resting baseline blocks (Arichi et al., 2012, 2010). In contrast, BOLD response to visual stimulation found that only newborns showed a positive BOLD response in the visual cortex while infants ages 2–12 months showed a generally negative BOLD response to the visual stimulus (Deen et al., 2017; Yamada et al., 1997). From fNIRS work, there is evidence for a positive hemodynamic response (i.e., increase in HbO) to auditory stimuli in temporal cortex (Homae et al.,

2014) and to visual stimuli in visual cortex (Grossmann et al., 2008) in children as young as 3–4 months. However, the shape and timing of the hemodynamic response changes significantly across the first year of life such that infants under 4 months of age exhibited a markedly slower and shorter hemodynamic response to auditory and visual stimuli than do older infants (Issard and Gervain, 2018). Taking these findings together, there are common themes that could lend insight into the development of resting baseline activation. First, the task-positive response compared to the task-negative response shifts across the first year of life, with newborns exhibiting a positive BOLD response to the task and older infants exhibiting and negative BOLD response to the task stimulation, likely due to the still developing neuronal-hemodynamic coupling. This suggests that there is a shifting baseline across infancy which extends into the toddler years. Second, that there is a typical stereotyped hemodynamic response present for motor cortex and not for visual cortex in infants is further evidence that cognition-specific cortical processes are not stabilized until late in development. Thus, not only can baselines not be directly compared across ages but they also cannot be compared within the individual child across domains of functioning. A task that has a motor control for an inhibitory condition, for example, must take this nonuniformity of development into account when interpreting results.

These studies of infant cognition also demonstrated an increase in baseline activity in older infants, at approximately the same age that the anterior FPN functional structure emerges (Gao et al., 2015a,b), suggesting a temporal association between resting baseline instability and FPN development in infancy. There is further evidence supporting this temporal association between the developing FPN and task-specific cognition in tasks collected from this young age from EEG work, which in turn supports that the development of resting functional networks are reflective of cognitive development in young children. For example, there is evidence that there is increased theta activity during sustained attention in infants compared to older children, the frequency band associated with higher cognition (Orekhova et al., 2006). In a study with 24-month-olds, toddlers who were rated by their parents as possessing better inhibitory control and attention shifting had higher EEG gamma power, suggesting that variations in resting-state electrical activity are associated with children's ability to regulate an FPN cognitive process (Benasich et al., 2008). Indeed, activity in the gamma frequency range has been linked with higher order cognitive processes in adults, such as attention (Ray et al., 2008), memory (Gruber et al., 2002), and language (Pulvermüller et al., 1996), all of which develop rapidly during early childhood. There is evidence that these shifts are specific to frontal and parietal regions and that theta synchronization during sustained attention emerges at 10 months of age (Xie et al., 2017). Taken together, this work suggests that development of resting networks is likely reflective of the developing cognition that those networks support, evidenced by the changes in electrical activity across infancy and toddlerhood that correspond to gains in cognitive control.

### 3.2. Unique activation effects in children during FPN-activating tasks

The emerging architecture of the FPN across childhood and the shifting (i.e., destabilized) role it plays in cognitive processes is evident in task-based neuroimaging work. The demands of tasks leveraging executive function—in which the FPN is expected to be more engaged during task than rest—often demonstrate developmentally-specific neural activity in children compared to adults. For this section, the type of baseline used—implicit baseline (baseline not modeled as a condition and condition main effects were used), explicit baseline (baseline modeled as a condition and condition main effects used), condition subtraction (e.g., higher cognitive load minus lower cognitive load), or baseline subtraction (i.e., condition minus resting baseline)—for each study are included in square braces for transparency. Notably, however, the studies included here are biased in the sense that primarily studies that have successfully found a condition effect in children are likely to be published. Thus, we almost entirely rely on studies that performed condition subtraction

within MRI studies while fNIRS and EEG studies are more varied in analysis and design. This pattern provides some further evidence for the main point of this section—FPN activity as probed by task-based neuroimaging is age and context specific. We posit that this lack of MRI work demonstrating baseline-dependent activation (i.e., condition activation as a “main effect” via implicit or explicit baseline) in children is potentially partially due to overlapping activation of resting baseline and FPN-activation task conditions during MRI acquisition as children engage greater top-down control in order to comply with task demands.

While the directionality of condition activation varies in hemodynamic studies, it is common to see a wider range of activation values in children than in adults (Adleman et al., 2002 [condition subtraction]; Kharitonova et al., 2015 [condition subtraction]; Tsujimoto et al., 2004 [condition subtraction]), spanning negative to positive effects of task and more activation of primary sensory and sensory integration regions of the cortex in children (Booth et al., 2003 [condition subtraction]; Crone et al., 2006 [condition subtraction]; Kharitonova et al., 2015; Scherf et al., 2006 [implicit baseline]) compared to adults in executive function tasks. For example, studies of working memory find increased prefrontal activation in adults while children tend to have less or negative prefrontal activation accompanied by increased parietal activation during the load portions of the trial (Crone et al., 2006; Kharitonova et al., 2015; Scherf et al., 2006) and inconsistent evidence of load-dependent effects (Kharitonova et al., 2015; Thomason et al., 2008 [baseline subtraction]). Studies of cognitive flexibility across preschool to adulthood find increasing activation of lateral prefrontal regions with age during flexibility trials (Marsh et al., 2006 [condition subtraction]; Moriguchi and Hiraki, 2011 [baseline subtraction]) with greater variability in activation in young children (Adleman et al., 2002). A study comparing inhibitory control between 9 and 12 year old children and adults found modest increased activation of limbic regions—including the amygdala, insula, medial PFC and the posterior cingulate—in children compared to adults during the inhibition trials however there were no significant differences in lateral prefrontal activation between the age groups (Booth et al., 2003). This lack of prefrontal activation during these cognitive tasks could be partially explained by the relative immaturity of the prefrontal cortex in children. Importantly, this lack of clear activation could be a byproduct of how activation is calculated in fMRI work. The general practice for fMRI analysis is to fit a response curve (the hemodynamic response function convolved onto a boxcar function of the task condition) to the obtained BOLD signal and obtain parameter estimates from this fitting. Next, researchers typically either explicitly subtract control or baseline parameter estimates from these condition parameter estimates, or they examine the main effect of the condition of interest using an implicit baseline for comparison. Both of these approaches presuppose that there would be more activation of the brain regions supporting task cognition during the trials rather than the resting baseline or control periods. In the case of young children asked to sit still in a scanner and play a repetitive and simplistic game, this assumption may be violated. If children are not actively engaged during both the task and resting baseline conditions, it is unlikely that prefrontal cortex activation would be reliably detected as the baseline periods likely require *more* top-down control than the task condition in order to focus on staying still. Additionally, task preparation during a resting baseline may recruit more neural resources than the task itself in young populations.

Interestingly, neuroimaging studies that either modify typical executive function tasks to be more colorful and engaging to children, or allow for more subject mobility such as using fNIRS and EEG, often report increased prefrontal activation in children during executive function even when utilizing baseline comparisons (Durstun et al., 2002 [implicit baseline]; Mehnert et al., 2013 [implicit baseline]; Perlman et al., 2016 [implicit baseline]; Quinoñes-Camacho et al., 2019 [condition subtraction]; Tsujimoto et al., 2004 [baseline subtraction]), though still with a wider range of activation in children compared to adults. For example, an fMRI study of inhibitory control that used Pokémon as stimuli found increased dorsolateral PFC activation in 6–10 year old children during

inhibition compared to adults (Durston et al., 2002 [implicit baseline]). An fNIRS study examining inhibitory control in 4–6 year old children and adults found that children had increased activation in both the lateral PFC and the parietal cortex compared to adults for both the non-inhibition and the inhibition trials (Mehnert et al., 2013 [implicit baseline]). Further, this study found increased within-region connectivity (parietal-parietal or prefrontal-prefrontal channels) in children and greater inter-region connectivity (parietal-prefrontal channels) in adults, consistent with resting state studies of the FPN. This developmental trend is evident in neuronal activity measured using EEG as well. For example, a study with 4-year-olds found that cognitive engagement was linked to increases in theta band activity with more cognitively demanding tasks eliciting more pronounced theta activity (Meyer et al., 2019 [condition subtraction & baseline subtraction]). Considering that theta activity is higher in infants than preschoolers (Orekhova et al., 2006), increases in theta band activity likely represent wide-spread engagement of the cortex (Gevins et al., 1997; Jausovec and Jausovec, 2004) which is generally increased in still-developing brains and shifts with gains in cognitive development. Contrasting the results of these studies with those previously discussed underscores an important point: the context under which children are assessed is critical for defining cognition that is occurring during resting baseline and resting state.

### 3.3. Behavioral evidence for destabilized baseline demand in children

The unequal demand placed on children during cognitive tasks is evident in behavioral reports, specifically high rates of movement (Satterthwaite et al., 2012; Van Dijk et al., 2012), supporting that there is more active cognition in younger children than in older teens and adults. Movement in pediatric populations is nearly always cited as a use for motion correction strategies, as discussed in the context of noise in section 4. While many studies do not report actual motion for their child and adult samples during acquisition, many, if not most studies, ultimately remove more child data than adult or adolescent data from analysis due to motion artifacts (Camacho et al., 2019a,b; Jonkman, 2006; Marek et al., 2015). Further, studies that do report within-condition motion in children often report significantly higher motion during baselines than during the more engaging task trials or movie (Cantlon and Li, 2013). We argue that this increased motion represents more than a lack of motor control. We propose that increased physical activity signals distinct cognitive processes occurring during these otherwise uneventful periods. Consistent with this, Greene et al. (2018) found that a behavioral intervention using movies instead of a fixation cross (both with and without feedback) greatly reduced motion during imaging for children under the age of 10 years but did not provide such a benefit for older children. A large study replicated this effect and found that children older than 12 years showed no difference in motion between being asked to rest versus watching a movie, while children younger than 12 years had significantly reduced motion when given a movie-watching activity to perform (Vanderwal et al., 2018). As discussed in Section 2, these ages correspond to the age in which the functional structure of the FPN emerges.

This temporal relationship between FPN development and physical behavior is also evident in studies of spontaneous behavior in children. It is widely observed that infants engage in spontaneous motor behavior such as kicking, waving, and reaching which decreases in frequency as they improve in gross motor control in the toddler years (Disselhorst-Klug et al., 2012; Robertson, 1982; von Hofsten, 2004). Further, developmentalists have long hypothesized that spontaneous movement in infancy accelerates not only gross motor development, but development of higher level cognition such as perceptual-motion mapping and self-regulation (Corbetta et al., 2000; Thelen, 1995). There is evidence to warrant extending this hypothesis to other spontaneous activity in early and middle childhood. One recent study of 4–8 year-olds found that at least 95% of their sample engaged in spontaneous, self-directed singing or speaking, the amount of which was inversely associated with performance on a variety of cognitive tasks (Thibodeaux et al., 2019), suggesting that the children who

engaged in less spontaneous behavior had more mature neural systems that support executive function. Taken together, this work supports our theory that activity at “rest” is developmentally expected and likely necessary to spur neural development. More systematic study of spontaneous movement in young children—and how it shifts across age—is needed to support our theory that young children are likely engaging in more overt, top-down cognitive control than adults are in order to comply with neuroimaging procedures.

## 4. The shifting nature of noise in developmental cognitive neuroimaging

Discussion of imaging developing cognition warrants careful consideration for the shifting nature of measurement and the measurement error—or noise—that accompanies it. In considering young children, there are many factors that are certainly shifting throughout development that bias estimates of brain structure and function, including: 1) partial volume effects within voxels of a given size will be greater in younger children than in older children; 2) brain region proportions shift across early childhood (e.g., relatively smaller cerebellum compared to cerebrum size in infants compared to individuals greater than age 8); 3) striking differences across age groups in methodology, ranging from collecting task and resting state data during sleep in infants and toddlers to using movies or having children focus their gaze on a cross hair; 4) shifts in global signal composition; and 5) changes in motion. All of the components contribute to error during acquisition and/or analysis, blurring what comparisons we can make across ages. The presence of an additional person in the magnetic field is also common during MRI acquisition from children under 5 years of age, as is movement during important calibration periods (a “jolt” at the onset of scanning sounds before the child settles). Global signal and motion have received the most attention in terms of methods development, therefore we focus this brief discussion on these two sources of noise.

### 4.1. Global signal

The nature of global signal noise—and how to account for it—has been a source of contention in the resting state field (Fox et al., 2009; Murphy et al., 2009; Murphy and Fox, 2017). In MRI, global signal is generally defined as the average signal across all voxels within the brain and therefore captures noise that is consistent across all acquired voxels. This includes nuances of the specific session noise (i.e., the magnetic field, subject motion) as well as physiological influences from cardiac pulsations and respiration (Birn, 2012; Chang et al., 2009; Power et al., 2017). These components of global signal shift in a nonlinear fashion across time, particularly in the first few years of life. Physiological noise in particular has been found to be the principle contributor to variance in resting state fMRI in adults within individuals, and removing this noise has improved reliability of connectivity estimates within and across subjects (Birn et al., 2014). As discussed in Section 2.2, there are major shifts in white and gray matter content as well as neurovasculature growth and expansion across early childhood. Children and infants under age 10 are also reported to have faster resting heart rates than adults (U.S. National Library of Medicine, 2019) with increasing heart rate variability across age (Galeev et al., 2002; Massin and von Bernuth, 1997). The impact of this cardiac development in early childhood on BOLD signal, however, has yet to be systematically studied. This lack of systematic study is likely partially due to the difficulty in collecting cardiac signals during fMRI scanning in young children as most MRI-safe devices are designed for adult-sized participants and with adult levels of tolerance in mind.

### 4.2. Motion

Subject head motion is idiosyncratic, context-dependent, and shifts in frequency and nature across age, inflating age effects in BOLD and



functional connectivity measures (Power et al., 2012; Satterthwaite et al., 2012, 2013; Van Dijk et al., 2012). As a result, fMRI work that seeks to compare individuals across age must perform careful motion control throughout their analyses, which was not the case for most studies prior to 2012 when the issue was brought front and center in developmental cognitive neuroscience. Towards this goal, extensive motion protocols have been developed including pre-appointment preparation (Camacho et al., 2019b; Howell et al., 2019), pre-scan motion practice in a mock scanner (de Bie et al., 2010; Perlman, 2012), real-time feedback in the form of scanner add-on software (Dosenbach et al., 2017), and in-scanner behavioral interventions (Greene et al., 2018). Since 2012, dozens of papers have been published proposing increasingly sophisticated motion de-noising pipelines (for a comparison of 14 proposed options, see Ciric et al., 2017), and groups continue to optimize denoising strategies for young populations. All of these approaches have been shown to dramatically improve usability of data collected from children, however it is still common for analyses comparing age groups to remove a disproportionate number of younger children from their analyses purely based on in-scan motion alone. We therefore urge the field to be strict in our methods for denoising our data and to take care to optimize denoising by characterizing each sample's unique noise and systematically removing it. Finally, it is critical that we transparently report 1) the average, range, and standard deviation of each motion parameter, 2) the associations of these parameters with age and any other variable of interest, and 3) the explicit steps taken—at all stages of data collection and processing—to denoise the neuroimaging data before conducting analyses.

## 5. What is rest in childhood?

Among several possibilities, we posit that rest, as it is currently studied in children, represents a period of increased inhibitory control demand. We theorize that this occurs as children are expected to wait for the next meaningful stimulus rather than experiencing a period of lower-order cognition, as is often assumed, and that this likely occurs during longer periods of rest (i.e., resting state and longer resting baselines). Decades of research on the development of executive function in children finds that attentional control tends to develop earliest, reaching adult levels around age 7–8, followed by cognitive flexibility reaching adult levels at around age 10–12, and both working memory and inhibitory control continuing to refine into adult levels in mid adolescence (Anderson, 2002; Luna et al., 2004, 2010). This implies that young children are still developing in all areas of executive function, which is likely reflected in their spontaneous neuronal activity as is observed in plasticity work (e.g., Jolles et al., 2013; Lewis et al., 2009). In the case of resting state, it is possible that the cognitive process being observed may in fact be cognitive control inhibiting physical movement in children rather than internally-directed cognition that is hypothesized to occur in adults. In children younger than 7–8 years, this inhibitory control is not likely sufficiently mature to suppress spontaneous behavior for the full span of a testing session (which typically last 30 min to an hour for children under the age of 10). This is evidenced by immature DMN and FPN function, the marked variability in executive function neuroimaging results, and in spontaneous speech and movement commonly observed in children. Thus, particularly in moments that are not occupied by specific instructions, children appear to be compelled to perform activity that drives development.

It is an open question as to whether or not variability in cognitive context influences functional connectivity measures. There is evidence in adults to suggest that functional network measurements are largely conserved across cognitive contexts (Finn et al., 2015; Gratton et al., 2018), however there is also evidence that variability in functional network measures between contexts can be important indicators of individual tendencies (Finn et al., 2017) and that changes in functional connectivity across adolescence and adulthood are context-dependent (Dørum et al., 2017; Murty et al., 2018). Dørum et al. (2017),

examined samples of younger and older adults and found that functional connectivity during a multiple object tracking task more accurately distinguished the two groups than did functional connectivity measured during resting state. While these samples were small (22 older adults and 25 young adults), a similar context-dependent association between functional connectivity and age was found in a longitudinal sample of 180 adolescents. Murty et al. (2018) found that functional connectivity between reward-sensitive regions that are known to continue developing across adolescence was only associated with age when functional connectivity was measured during a reward task but not during resting state. Taken together, with evidence that an individual's functional connectivity can be predictive of activation (Finn et al., 2017), these data suggest that functional connectivity between cognitive contexts may play an important role in our understanding of cognitive development. It is entirely possible that further research conducted on large samples—such as those in the midst of early releases like the ABCD study—may prove that functional connectivity does not meaningfully differ across contexts across the lifespan, however the consequences of context on activation are likely significant across development. Thus, the association between functional connectivity and context-specific activation must be carefully examined across development to fully map the developing brain.

In the case of longer periods of resting baseline (e.g., inter-block intervals), children are potentially suppressing developmentally-expected behavior in order to comply with task instructions. Increased prefrontal activation may underlie this inhibition, especially in children under 10 years old (Fishburn et al., 2019; Kharitonova et al., 2015; Li et al., 2017) in the process of experiencing the largest gains in development of cognitive control. This inhibitory control is further layered in with task-contextual demand such as preparing to find a specific stimulus on the screen or to make a movement. Depending on the complexity of the task, this can lead to increased prefrontal activation during resting baseline, making it difficult to justify continuing to refer to these periods as baselines and difficult to qualify these resting baseline periods as “equalizers” across development. In the case of shorter periods of resting baseline, however, it is less clear what cognitive state a young child is likely in. In adults, there is evidence that short resting baseline periods are used for cognitive preparation before the next task item is presented (Gallivan et al., 2011; Hester et al., 2004; Sala-Llonch et al., 2012; Simon et al., 2002), a process that is still developing in adolescence (Church et al., 2017; Flores et al., 2009; Hwang et al., 2016). These studies used short periods to model this preparation (0.3–2 s), and it is unclear if these short periods would require young children to engage inhibitory control systems as longer inter-block intervals (e.g., those 10 seconds or longer) or resting state scans (6 minutes or longer) likely do. Thus, it is possible that short intervals are not equal across development for the opposite reason—adults likely engage cognitive control regions more than children do during brief resting baselines in order to prepare for the upcoming cognitive demand. These theories concerning cognition during resting state and resting baselines, however, have yet to be explicitly tested, and we urge the developmental cognitive neuroscience community to thoroughly interrogate the activity and behaviors present during rest in children under the age of eight.

## 6. Future directions: Re-framing the meaning of “rest” in childhood

In this section we discuss approaches for future research in developmental cognitive neuroscience in children and considerations for both study design tailored to the construct of interest and for interpreting network activation during resting state. In the context of experimental design, we expand on previous recommendations (Church et al., 2010) for imaging youth generally by offering advice more specific to children under the age of 8 years old. First, we suggest reducing the cognitive burden on school-aged children by either allowing for more mobility or making tasks more colorful, engaging, and child-friendly. Engaging tasks are easier for young children to focus on by engaging automatic



(bottom-up) attention processes and therefore allowing children to more naturally stay engaged for longer periods of time before top-down processes are required to stay engaged in the task. To accomplish this, affective stimuli could be presented in the form of video clips (e.g., Camacho et al., 2019a; Karim and Perlman, 2017; Richardson et al., 2018), for example, or basic stimuli can be replaced with more complex pictures and sounds that follow a loose story (e.g., Fishburn et al., 2019; Perlman et al., 2014; Quinoñes-Camacho et al., 2019). Thus, modifying tasks to be more naturally engaging and colorful can serve to reduce the hypothesized increased engagement of the FPN required for top-down control that would be required for children to stay engaged in a repetitive task. For very young children such as toddlers and preschoolers, however, even colorful and exciting games still likely require increased engagement of the FPN as they typically last more than 5 min in order to capture enough trials for analysis. In this case we suggest repetitive testing of the same task (with breaks in between) and an increased sample size to allow for extra power in the context of short data collection periods. This is a common strategy in developmental fNIRS studies (Biondi et al., 2016; Fishburn et al., 2019; Quinoñes-Camacho et al., 2019). We also suggest, when studying children in a restricted age range, that future task design consider that baseline conditions subtracted from the condition of interest be designed to engage the intended neural system at a minimal level in order to provide a “cognitive break” while still constraining cognition. For example, in a working memory task a heavy load can serve as the condition of interest with a light load serving as a comparison condition (e.g. 1 back vs. 3 back; short vs. long time to recall). This removes the interpretation of the cognitive systems involved in rest as a confound of the experiment. When studying children across larger age ranges (such as comparing toddlers to preschoolers, children to adults, etc.) we suggest that researchers follow the recommendations in Church et al. (2010) and perform between group comparisons for all tested conditions including resting baseline. Testing associations between each condition and age or age group separately would eliminate the concern that subtractions between condition and resting baseline may obscure activation associated with the task condition of interest. Finally, we suggest that resting state studies across ages consider a low cognitive engagement video stimulus in order to better approximate the constant information processing and behaving that we have discussed previously as typical of children. This has been suggested by other researchers in the context of neuroimaging (Greene et al., 2016; Vanderwal et al., 2015) and is also typical of physiological studies in young children requiring a resting baseline (Calkins, 1997; Calkins et al., 2001; Perlman et al., 2008). By shifting the standard resting stimulus in the field to a low stimulation video, we can obtain more consistent network measurements in adolescents and adults (Hasson et al., 2010) as well as improve comparisons across samples and therefore improve comparisons across age.

Within the context of experimental result interpretation, we first call upon the research community to explicitly investigate maturational effects in resting baseline through longitudinal study and report findings on this condition regularly. That is, we suggest a movement away from a baseline condition as an implicit “equalizer” and request that future manuscripts specifically examine developmental change in resting baseline alongside a task condition, with full reporting of activation associations with age for each “resting” and “active” condition of the task. Second, we suggest that authors carefully consider the theoretical conceptualization of a resting baseline in their tasks (e.g. inhibition, attentional shifting, motor preparation) and discuss its implications within the context of the results. We note that the theoretical interpretation of a resting baseline condition will be specific to the context of the experiment and the age of the child subjects. Thus, the reframing of the meaning of rest across developmental studies may vary widely. Third, we emphasize the rapid neurodevelopment across early childhood—particularly in infancy and toddlerhood—and suggest that researchers design their MRI protocols of this age for depth rather than breadth. For example, a study seeking to examine activation to an auditory task in infants would benefit from also imaging cerebral

neurovasculature and reporting tissue perfusion of the regions in which task-dependent activity is observed. These additional data may increase the usefulness of this work in BOLD imaging as new methods for capturing activation and hemodynamics are developed in MRI and a more complete picture of emerging neuronal-hemodynamic coordination during this age period is developed. Fourth, we urge the community to continue to push for creative solutions to enable neuroimaging research in early childhood. For example, with cameras in the scanner becoming more commonplace, researchers could potentially rate spontaneous behavior during MRI scanning. These data would provide insight into 1) how children may behaviorally adapt to the heightened demand during neuroimaging and 2) if spontaneous behavior shifts across development within the MRI scanning environment as it does in behavioral observations. Finally, we suggest open discussion related to this topic both in print and at scientific meetings as the field moves from a state of flux in the implementation and interpretation of resting state and resting baselines in scientific research.

### Declaration of competing interest

None.

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