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Review

A decade of infant neuroimaging research: What have we learned and where are we going?

Atiqah Azhari[1], Anna Truzzi[2], Michelle Neoh Jin-Yee[1], Jan Paolo Macapinlac Balagtas[1], Tan Hui Ann Hannah[1], Goh Pei Lin Pamela[1], Ang Xin Hui Anais[1], Peipei Setoh[1], Paola Rigo[3], Marc H. Bornstein[4,5] and Gianluca Esposito[1,6]

[1]Psychology Programme, School of Social Sciences, Nanyang Technological University, Singapore
[2]Trinity College Institute of Neuroscience, Trinity College Dublin, Ireland
[3]University of Padua, Italy
[4]Eunice Kennedy Shriver National Institute of Child Health and Human Development, USA
[5]Institute for Fiscal Studies, United Kingdom
[6]Department of Psychology and Cognitive Science, University of Trento, Italy

A B S T R A C T

The past decade has seen the emergence of neuroimaging studies of infant populations. Incorporating imaging has resulted in invaluable insights about neurodevelopment at the start of life. However, little has been enquired of the experimental specifications and study characteristics of typical findings. This review systematically screened empirical studies that used electroencephalography (EEG), magnetoencephalography (MEG), functional near-infrared spectroscopy (fNIRS), and functional magnetic resonance imaging (fMRI) on infants (max. age of 24 months). From more than 21,000 publications, a total of 710 records were included for analyses. With the exception of EEG studies, infant studies with MEG, fNIRS, and fMRI were most often conducted around birth and at 12 months. The vast majority of infant studies came from North America, with very few studies conducted in Africa, certain parts of South America, and Southeast Asia. Finally, longitudinal neuroimaging studies were inclined to adopt EEG, followed by fMRI, fNIRS, and MEG. These results show that there is compelling need for studies with larger sample sizes, studies investigating a broader range of infant developmental periods, and studies from under- and less-developed regions in the world. Addressing these shortcomings in the future will provide a more representative and accurate understanding of neurodevelopment in infancy.

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1. Introduction

With the advent of technology to image the brain, neuroimaging research has contributed immensely to understanding human brain structure and function. Neuroimaging has become a primary tool in neuroscience research and involves any technique that allows the study of brain structure or function, temporal processing and spatial localization of cerebral function (Brammer, 2009).

The application of neuroimaging techniques to research in infant populations is crucial to advance our understanding of brain development and corresponding developmental trajectories of motor, perceptual, social, and cognitive skills (Raschle et al., 2012). Neuroimaging provides information about human brain development that is difficult to obtain from behavioral studies. In developmental science, imaging infant brain structure and function can be used to predict developmental trajectories. For example, in a longitudinal study Ichikawa et al. (2019) used functional near-infrared spectroscopy (fNIRS) to chart the emergence of milestones in facial processing. The field of infant neuroimaging has received growing interest, and the purposes of this review are to characterize and provide perspective and insight into trends in this burgeoning literature and, consequently, examine what these trends imply and directions of future research. The review is structured as follows: first, an overview of the neuroimaging modalities employed in this research, followed by an overview of some key characteristics of the current literature reviewed and finally, a discussion on what the findings of this review may mean and suggestions for moving the field forward.

2. Four neuroimaging techniques

Infant neuroimaging has been limited by challenges posed by infants in experimental settings, including practical and procedural difficulties such as sustaining the attention of easily irked infants, artefact movements diminishing the quality of data, and the need for non-invasive procedures (Raschle et al., 2012). In spite of these difficulties, application of neuroimaging research in infants has increased and has proved invaluable in providing insight into brain plasticity during development, developmental trajectories, and understanding the human connectome (Keunen, van den Heuvel & Collin, 2018). In this respect, a number of imaging modalities are currently employed in the infant literature: (i) EEG, (ii) MEG, (iii) fNIRS, and (iv) fMRI.

2.1. EEG

Electroencephalography is an electrophysiological method to monitor electrical activity in the brain through electrodes on the scalp. The primary source of EEG signals is synchronized synaptic activity in populations of cortical neurons. EEG is able to detect both tangential and radial currents and thus includes signals from most areas of the cortical surface. Event related brain potentials (ERPs) are averaged electrical brain responses relative to a specific known event or stimulus (Blackwood & Muir, 1990) and are used to isolate brain activity occurring at a specific moment to a specific stimulus. EEG has a high temporal resolution of milliseconds, which allows it to capture dynamics of evoked responses (Glover, 2011). Advances in recording methods and signal analysis have made EEG one of the foremost imaging methods in infant research, allowing for better source localization and acquisition of infant brain connectivity and mapping of neural networks (Vanhatalo & Fransson, 2016).

The application of EEG in infant studies initially originated in studying the functions of infants' central nervous system in understanding the neural bases for various perceptual and cognitive processes. For example, a number of ERP studies have been conducted in infants to investigate the neural correlates of face recognition in infancy (see de Haan, Johnson, & Halit, 2003, for review). Two face-sensitive infant ERP components were identified (N290 and P400) in a study where faces elicited a P400 occurrence

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and the N290 response differed in amplitude between monkey and human faces (de Haan, Pascalis, & Johnson, 2002). Halit, de Haan, and Johnson (2003) then showed that these components have higher specificity to upright human faces (as adults) in 12-month-old infants compared to 3-month-old infants, indicating that both components integrated during development and preceded the adult equivalent N170 component. Another area where ERP studies have been conducted in infants is in auditory recognition memory. An initial study investigated the development of auditory recognition memory for the maternal voice and found that positive components (denoted P2) were evoked in newborn infants towards both maternal and stranger voices whereas a negative slow wave was present for a stranger's voice (de Regnier et al., 2000). Results from a subsequent study then indicated that brain maturity and postnatal experience were important factors in infant auditory recognition memory by comparing ERPs in preterm infants, full-term newborn infants and full-term infants with 2 weeks of postnatal experience (de Regnier et al., 2002). These studies reveal how results from EEG studies can provide insight into development of perceptual systems and differences between the neural mechanisms of adult and infant brains.

Another example where the EEG has been applied is research on infant motor system development. Monroy, Meyer, Schröer, Gerson and Hunnius (2019) investigated the effect of novel perceptual information about action sequences in generating action predictions in infants by measuring the infant mu rhythm, which is an index of motor activity (Marshall & Meltzoff, 2011; Southgate, Johnson, Osborne, & Csibra, 2009). By making use of a developmental approach that only included visual statistical learning in a naïve group of participants, this study provided support for theories in which the motor system is said to underlie action prediction.

Other than the use of resting state EEG and ERPs in infant research, another approach is the analysis of event-related oscillations (EROs). EROs are bursts of EEG at particular frequencies which have been associated approximately in time to the task or stimulus presentation event. Neurons spontaneously produce oscillatory activity at frequencies above 20 Hz (Llinás, 1988), while sensory stimuli can elicit such oscillations in the gamma band frequency of 20-80 Hz. The synchronous firing of a large number of neurons at the same frequency can be recorded with conventional EEG techniques, and the EEG signal can be analysed in both the time and frequency domain. A study applying ERO analysis investigated gamma-related oscillations in infants related to binding – the brain's ability to knit together different stimulus features coded at early stages of vision – while infants viewed static illusory objects (Csibra, Davis, Spratling, & Johnson, 2000). Here a time-frequency analysis was conducted on the gamma-band activations and revealed differences in activation patterns between 6- and 8-month-old infants. This study shows how patterns in EROs analysis can indicate development of cognitive processes in infants. Another study making use of ERO analysis investigated electrophysiological responses in infants towards object occlusion (Kaufman, Csibra, & Johnson, 2003) and found higher gamma-band oscillatory activity during an unexpected object disappearance compared to an expected object disappearance. This observed gamma activity was then proposed as the neural basis for object permanence in infants. This study shows how ERO analysis can be used to uncover underlying neural mechanisms of infant cognition.

Dual EEG, where the brain activity of two individuals is recorded simultaneously, has been used to investigate the neural activity in adult-infant dyads in the same experiment. This design can be used to observe neural synchrony. For example, a study investigated adult gaze on neural coupling in adult-infant dyads during both screen-based and live communication interactions. The study involved two experiments where infants viewed videos of an adult singing nursery rhymes or the same adult in a live context with either a direct or indirect gaze. Significant neural synchrony between infants and adults during social interaction was observed. Adult direct gazes

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lead to higher interpersonal neural synchrony in both the theta and alpha frequency bands as compared to an averted gaze (Leong, Byrne, Clackson, Georgieva, Lam, & Wass, 2017). In addition, bidirectional patterns of influence were observed between parent and child only during live social interactions as seen in the stronger influence that the adult had on the infant than vice-versa during direct gaze (Leong et al., 2017). This study showed how dual EEG can be a useful methodology in investigating the neural correlates of temporally contingent social interactions such as the mother-child interaction.

A major drawback of EEG is that readings are prone to movement artefacts, such as eye blinks, muscle movements, and head turns, that lead to low signal-to-noise ratios and result in the need to remove artefactual trials. This limitation is pronounced in infants as they hardly remain still. The small amplitude or noise of an individual ERP further undermines signal quality and increases the number of trials required during experiments. Finally, EEG has poor spatial resolution and limited source localization (compared to the fMRI), as it is difficult to specify which brain area(s) gives rise to the ERP as ERPs only provide information about activity at the cortical surface.

2.2 MEG

Magnetoencephalography (MEG) measures changes in the oscillation of a magnetic field that stems from the movement of ions along electrochemical gradients of neural cells (Cohen, 1991). The field produced by an individual neuron may be weak, but the clustering of several neurons within a delimited region yields a sufficient magnetic field that may be detected from outside the head. This principle of MEG serves as its main advantage, enabling researchers to measure brain activity directly from the source (brain) rather than from proxy signals in the sensor space. MEG has good temporal resolution (i.e., millisecond) similar to EEG. As magnetic fields are less likely to be affected by resistance due to the skull or scalp, MEG has a better spatial resolution compared to EEG. When MEG is used in concert with structural magnetic resonance imaging (sMRI), higher spatial resolution can be achieved (Chen et al., 2019). These advantages have led MEG to become a popular method for studying brain activity in adults, and, more recently, in children. The minimal set-up time and emergence of infant whole-head MEG systems render MEG as a candidate for studying brain activity in awake infants (Chen et al., 2019). An example of how infant MEG is used in research looking into early experience and development of temporal structure processing is Zhao and Kuhl (2016) who examined the effects of a laboratory-controlled music intervention on infants' neural processing of music. Infants' neural processing was assessed from MEG measurements of their mismatched response to a typical oddball task. This study offered evidence for the effect of music interventions on neural processing of temporal structural information.

MEG possesses several disadvantages, the first of which is its limited sensitivity to currents that flow tangent to the surface of the head (Williamson & Kaufman, 1990). As such, sulcal brain activity is not reliably captured. Because the traditional MEG detects electromagnetic changes using helmet sensor array hardware, the distance between the source and detector is greater for the MEG compared to EEG, which uses scalp-placed electrodes. This requirement adds to the lack of depth sensitivity of the MEG, which is beginning to be surmounted with smaller-scale MEG that minimizes source-detector distance. Due to the shorter necks and smaller heads of infants, existing MEG hardware designed for adults is not optimal for infants, and a specially designed MEG sensor helmet is also required specifically for use in infant neuroimaging which is not as commonly available (see Okada et al., 2016). Nonetheless, advances in preprocessing and analytical techniques have enabled recording MEG signals from deeper brain areas. For instance, MEG can be used to measure auditory brainstem responses (ABRs), which are usually recorded by the EEG (Coffey et al., 2016). MEG measurements are also susceptible to artefacts caused by movement. While software solutions for head movement

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compensation (Kuhl, Ramírez, Bosseler, Lin, & Imada, 2014) and hardware solutions, such as adjustable head casts for constant repositioning, are available, they remain limited (Meyer et al., 2017). Last, the MEG system is both expensive and incurs high operating costs while requiring training of personnel in utilising this system.

2.3 fNIRS

fNIRS is an optical imaging technique that takes a hemodynamic approach to neuroimaging by monitoring regional tissue oxygenation. The working principle is that hemoglobin chromophores absorb light selectively, and changes in chromophore concentrations can be quantified from light emitted from sources and received by detectors on the scalp, serving as a proxy of metabolic demand in neural cells (Lloyd-Fox et al., 2010). fNIRS measures relative oxygenated and deoxygenated hemoglobin concentrations that indicate cerebral activation and deactivation. Measurements are taken using detectors placed on a cap where source-detector pairs form channels. The portability and multi-channel design of fNIRS allows it to be relatively free of motion restrictions and lends it high ecological validity (see Nishiyori, 2016). The tolerance of the fNIRS system to movement has made it one of the key tools in infant neuroimaging research (Vanderwert & Nelson, 2014; Boas, Elwell, Ferrari, & Taga, 2014; Wilcox & Biondi, 2015). For instance, fNIRS has been used to examine neural development in facial processing (Ichikawa et al., 2010; Ichikawa et al., 2013; Ichikawa et al. 2019; Nakato et al, 2009; Nakato et al., 2011a; Nakato et al., 2011b). In a longitudinal design, Ichikawa et al. (2019) investigated the development of certain brain regions and showed that infant face processing occurred for frontal before profile faces. These studies demonstrate the usefulness of fNIRS in experimental paradigms that require the infants' prolonged attention to investigate milestones in socio-cognitive processing.

Hyperscanning involves simultaneous recording from two or more brains and allows for the investigation of interpersonal neural correlates, which is particularly relevant in the area of social neuroscience. The term was first introduced in Montague et al. (2002) who used the fMRI, but hyperscanning methodology has emerged for the other modalities as well. Hyperscanning is increasingly applied to examine social interactions by determining neural synchrony – the synchronisation of brain activity between two interacting individuals. Combined with the tolerance to movement, fNIRS is well suited to investigating parent-infant synchrony and determining the role of parent-infant synchrony in the development of social outcomes in infants. For example, Minagawa (2016, discussed in Minagawa, Xu, & Morimoto, 2018) found the largest mother-infant synchrony in the orbitofrontal cortex when mothers, compared to experimenters, held their children. This example demonstrates the immense potential of the fNIRS hyperscanning methodology in providing insight into neural mechanisms that maintain the unique mother-infant relationship.

Like other imaging methods, fNIRS has its shortcomings. Compared to the EEG, fNIRS possesses greater spatial resolution, although it is deficient relative to the temporal precision of EEG. Contrasted with fMRI, fNIRS boasts greater temporal resolution although it lacks the spatial accuracy of fMRI. While fMRI allows for exact mapping of brain structures, fNIRS localizes brain areas based on the loci of channels. Moreover, fNIRS is only able to record signals from cortical surfaces and is limited by the scatter and attenuation of photons (Glover, 2011). Investigation into deeper subcortical brain structures is thus unattainable. In spite of these weaknesses, fNIRS provides complementary spatial knowledge to the temporal strength of EEG studies, and its portable and flexible use allows it to be implemented in a greater variety of experimental paradigms compared to fMRI (Grossmann, 2015).

2.4 fMRI

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Functional Magnetic Resonance Imaging (fMRI) is one of the most prominent and widely used neuroimaging tools. This imaging method is capable of functional activity of the brain through blood oxygen level dependent (BOLD) signals. Despite its early well-established roots, the use of fMRI in infant research has only fully emerged in recent decades. The advent of fMRI studies on infants heralded new experimental paradigms that facilitated infant neuroimaging research. For instance, issues of movement and remaining still during the scanning duration were addressed by conducting fMRI scans with infants during natural sleep (Anderson et al., 2001; Dehaene-Lambertz, 2002). Advances in fMRI have allowed scanning awake and behaving infants (Ellis & Turk-Browne, 2018) with only two recent studies involving awake infants (see Deen et al., 2017; Biagi et al., 2015) while other studies have reported very high attrition (Leroy et al., 2011; Dehaene-Lambertz et al., 2010).

fMRI measures the whole brain and has a relatively high spatial resolution (Logothetis, 2008), with a typical pixel size of 3-4 mm. Functional activity of the infant brain has been investigated in two ways: (i) task-based fMRI allowing examination of brain responses to specific aspects of the environment and (ii) resting state functional connectivity MRI which assesses the intrinsic functional organisation of the brain (Graham et al., 2015). The high spatial resolution of fMRI means that studies can look into the functional connectivity of specific brain areas as well as the changes in connectivity. For example, Lordier et al. (2019) tested preterm infants who received a music intervention with different kinds of music and found increased connectivity in cerebral regions implicated in tempo and familiarity processing compared to full-term or preterm infants who did not receive the intervention. This study determined the involvement and connectivity between auditory cortices, the thalamus and striatum, in music processing and the contribution of an early music intervention to cortical processing of music. Infant fMRI studies are thus ideal for investigating neurodevelopment in terms of both the timing of emergence of various neural processes and associated changes in functional connectivity that occurs during this unique early developmental period. This study demonstrates the role of fMRI as a key modality in investigating the functional connectivity of the brain and infant fMRI studies as an important source of information regarding the development of connectivity networks and environmental factors affecting them.

Despite its long-standing use in imaging research, the fMRI faces several limitations. Due to the time delay associated with the collection of BOLD signals, the fMRI has low temporal resolution (Glover, 2011). In addition, similar to MEG, fMRI machinery is not only expensive, but it is also a costly procedure requiring trained technicians to conduct the MR imaging. The ecological validity of fMRI studies is also severely limited as contraindications of being in a magnetic field, movement restriction, noise of the scanner, and the supine position of participants are factors that limit the kinds of tasks and populations that can be studied using fMRI (Logothetis, 2008). Infants in particular do not abide by the motion restriction required of a scan, and adults and infants alike may find the noise of the scanner distracting. As mentioned earlier, this means that infant studies involving fMRI are most successful when infants are asleep or sedated, a circumstance that severely limits the types of research can be conducted. For example, visual neuroscience and other experimental task paradigms involving visual stimuli or attentiveness/wakefulness are not viable. However, recent advances have allowed researchers to utilise resting-state fMRI to investigate functional connectivity of the fetus *in utero*. Unlike task-based fMRI, resting-state fMRI does not require active participation from the participant, and spontaneous activity in functional networks continues to occur (van den Heuvel and Hulshoff Pol 2010; Rosazza and Minati 2011). Such technical advances may overcome some of the limitations of fMRI applied to infant and even fetal populations (Biswal et al. 1995).

3. Aim of the current perspective

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Neuroimaging has been applied to a wide range of research objectives in infancy. This systematic review focuses on infants aged newborn to 24 months, studies involving experimental paradigms, and studies conducted from 2008 to 2019. We examined trends in recent infant neuroimaging literature with respect to sample size of studies, age of infants, geographical distribution of studies, study design (i.e. longitudinal), and purpose of studies (i.e., clinical or non-clinical). We chose these parameters to better understand the sample characteristics (e.g. average age, location) from which information regarding early neurodevelopment is typically drawn, evaluate the accuracy of findings given the sample sizes of studies, and examine the frequency at which different imaging techniques are employed to track longitudinal changes and pathological development. We also suggest gaps to be addressed in studies going forward.

4. Methods

The Scopus database was used to glean articles relating to neuroimaging studies of infant populations from the decade 2008 to 2019. Four database searches were made using the Boolean operators "AND" and "OR": 1) (EEG OR electroencephalography) AND (infant OR children); 2) (MEG OR magnetoencephalography) AND (infant OR children); 3) (fNIRS OR (near AND (infrared OR infra-red) AND spectroscopy)) AND (infant OR children); and 4) (fMRI OR (functional AND magnetic AND resonance AND imaging)) AND (infant OR children). These searches generated an extensive list of records (N=21,486), which were subsequently screened based on two search criteria: 1) records should include infants of ages newborn to 24 months and 2) records should consist of imaging techniques which were utilized for empirical paradigms. Records were split into the four categories of imaging methods of interest before they were screened on the two inclusion criteria. All records were screened according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines as illustrated in Figure 1 (Moher et al., 2009). A total of 710 records were eventually retained for analysis (see DOI: 10.21979/N9/HLICMO for database of full references).

From the 710 records included, sample size of the study was obtained to discover the scope of the study, average age of infants was obtained to evaluate the stage of infant development at which the study was conducted, and information regarding the geographical location of the study was extracted to examine the socio-cultural context of the study. Studies were noted for whether they adopted a longitudinal paradigm or were conducted for clinical research so as to ascertain the purposes of applying neuroimaging methods. A study was coded as longitudinal if it included a follow-up study that was conducted on the initial sample after the first study was completed (e.g. a study where infants were tested at 6 months of age and later again at 12 months of age). R Software (de Micheaux, Drouilhet, & Liquet, 2014) was used to produce density kernel plots, geographical distribution maps, and bar charts.

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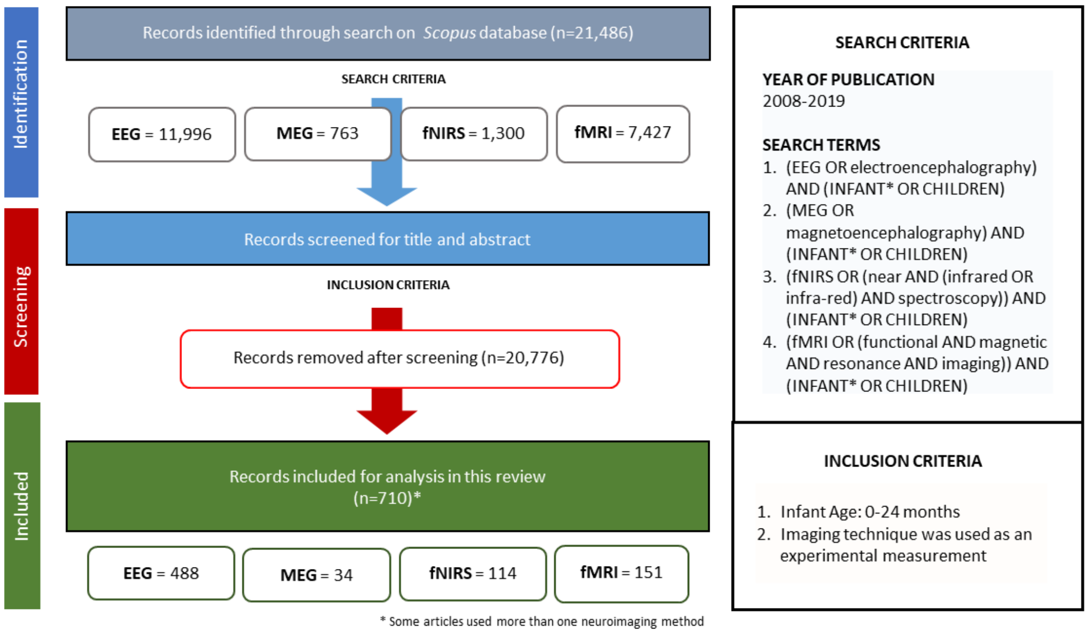

Figure 1. PRISMA Flow for Inclusion of Records. Records were identified on Scopus database from four sets of search terms before they were screened for their title and abstract, followed by inclusion criteria: 1) newborn to 24 months and 2) imaging technique as an experimental measure. Records which did not meet these criteria were removed, and a total of 710 records were derived for qualitative analysis.

5. Overview of Current Literature

Neuroimaging of infant populations has dramatically altered the lens through which we investigate infant development. Neuroimaging research in infants has examined into topics in developmental and cognitive neuroscience, namely in studying and understanding the neural bases of human perception, cognition, and emotion. Studies have looked into areas including but not limited to the understanding of developmental processes during infancy, such as visual and auditory perception, facial perception, motor development and acquisition of language, as well as social cognition functions, such as mentalising. We attempted to evaluate progress in this field across a 10-year period, exploring the distribution of EEG, MEG, fNIRS, and fMRI from geographical and temporal perspectives.

5.1 Trend across years

Each neuroimaging method showed a unique trend of utility over the ten-year period. Figure 2 illustrates a ridgeline distribution plot for each method. The first observation to note is the overall decreasing trend of fMRI, EEG and fNIRS studies from the peak in 2009 to the present. Second, the lowest point of the distribution plot for EEG, MEG and fMRI in 2017 coincides with an increase in the use of fNIRS which suggests a potential shift in the choice of method for infant brain studies.

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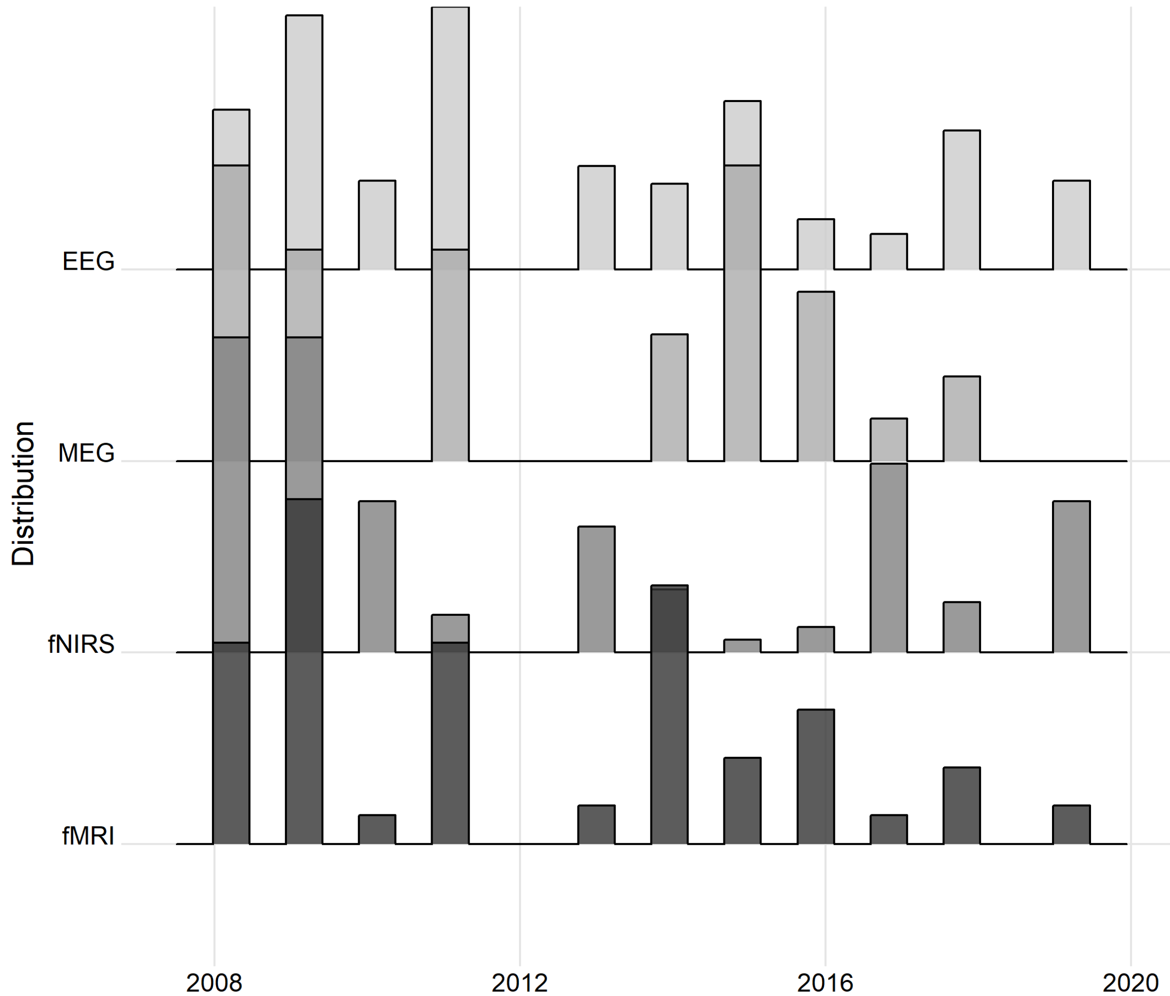

Figure 2. Distribution plot across ten years. Ridgeline distribution plot depicting distribution curves for each neuroimaging method from 2008 to 2019.

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5.2 Age of infants

Infancy is a time of rapid and crucial developmental changes, but samples often consist of only key milestone ages. We investigated the average age, minimum age, and maximum age of infants within each study according to each neuroimaging device, as illustrated in Figure 3. Peaks of average age of infant (Figure 3a) suggest that the developmental periods in infancy that are commonly investigated fall around birth and at 12 months. This observation indicates that studies show great interest in the condition of the brain around birth and at the accumulated development of the brain at the end of the first year of life. However, the plots of minimum and maximum ages of infants (Figures 3b and 3c) each depicts a peak at in newborns, suggesting that one-time data collection predominantly occurs on newborns. Figure 4c shows another prominent peak at 24 months which suggests that a large proportion of studies continues to investigate infant development beyond the first year of life. Moreover, the tapering number of studies after the first year in Figure 3c suggests that, beyond the first 12 months, researchers are likely to investigate infant development till the end of the second year. The pronounced average age at 12 months is likely due to the high occurrence of longitudinal studies spanning from birth to 24 months. EEG is the most frequently used device across all ages, which suggests that knowledge regarding intermediary and milestone phases of infant neurodevelopment largely revolves around electrical activity, with less information acquired on spatial, anatomical, and functional characteristics of brain development.

5.3 Effect sizes of studies

Effect size measures the magnitude of difference between groups and addresses a more sophisticated question of the extent to which an effect is observed, instead of simply identifying whether an effect is present (otherwise ubiquitously reported as p-values in literature). The ‘pwr’ package in R was used to calculate Cohen’s *d* effect size with the following parameters: p = 0.05 and power = 0.80. Out of 710 studies, 89 studies were omitted from this analysis due to insufficient or unclear data regarding the *M* and *F*-values . The mean effect size across the studies is d = 0.74, which is considered a medium effect size as it falls between d = 0.5 to d = 0.8.

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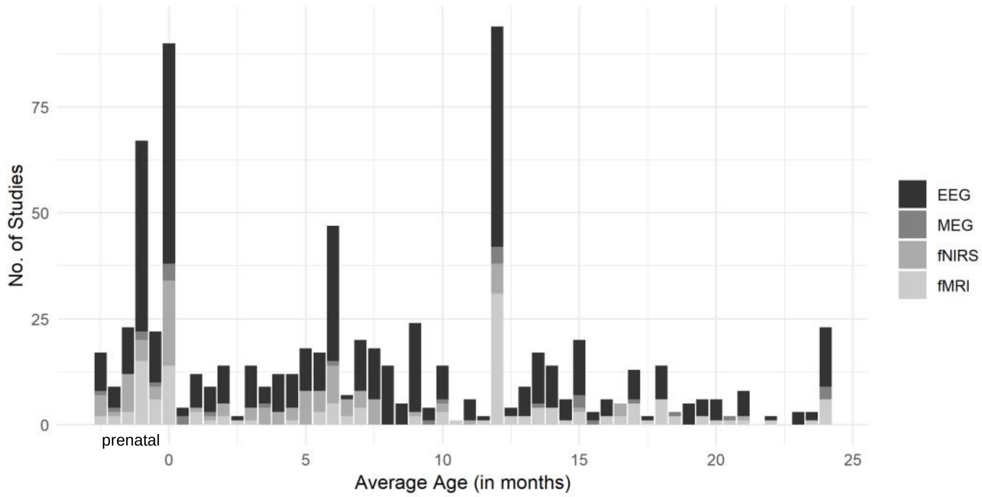

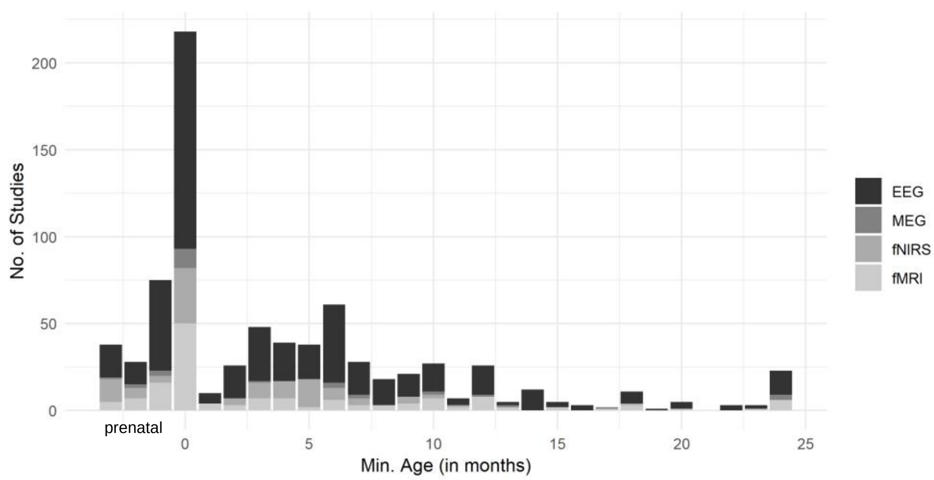

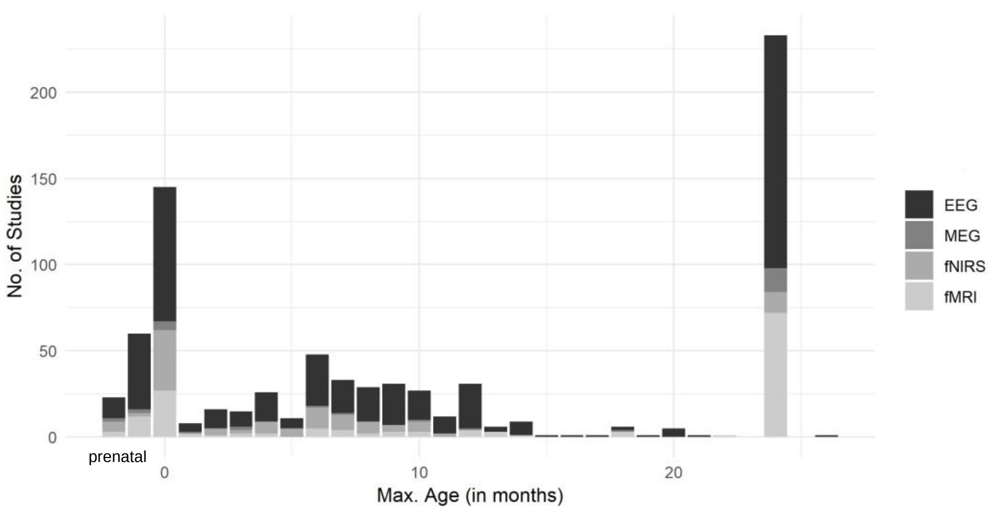

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Figure 3. Age of infants by method. Bar plots depicting the **a)** average age (top), **b)** minimum age (middle) and **c)** maximum age (bottom) of infants in each study against number of studies across neuroimaging methods. Age < 0 refers to studies conducted prenatally.

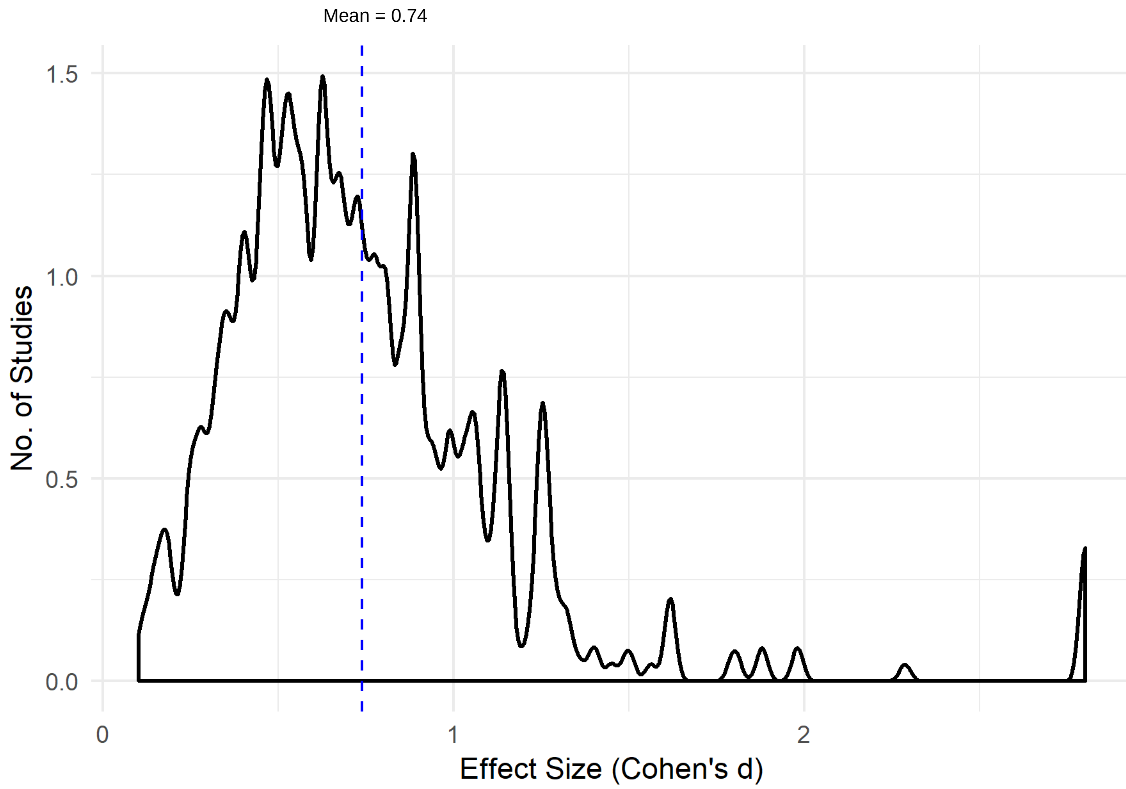

Figure 4. Effect size. Density plot depicting effect size against number of studies.

5.4 Geographical Distribution

We identified the location where each type of neuroimaging study was conducted and plotted locations on world maps (Figure 5). Except for Africa, studies have been conducted in nearly all parts of the world using EEG, MEG, fNIRS, and fMRI. A disproportionately great number of studies comes from North America and the United States. However, Japan has conducted similar amounts of experiments as the United States for fNIRS ($N_{\text{United States}}$ = 24, N_{Japan} = 25). To compare neuroimaging methods within a region, we plotted the proportion in which each method is used in Figure 6a. At the regional level, North America published the most studies, followed by Europe, Oceania, Asia and Africa. A similar pattern of neuroimaging method is seen across all continents, whereby EEG is the most widely used method (Figure 7b). In Japan, the most commonly employed neuroimaging method is the fNIRS. The enhanced usage of fNIRS devices in Japan could possibly be attributed to the presence of leading fNIRS manufacturers in Japan such as Shimadzu Corporation and Hitachi High-Technologies Corporation.

5.5 Longitudinal Studies

We investigated the use of neuroimaging methods in longitudinal studies. A total of 191 studies employed longitudinal designs in which EEG was most utilised (N=132), followed by fMRI (N =42), fNIRS (N =15), and MEG (N =2). Figure 8 depicts the age range of infants in each study according to neuroimaging method. The shorter

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duration of studies within the first year suggests more selective investigation of infants that fall within a specific targeted age range. This trend may be symptomatic of less temporal resolution of investigation of milestones in the second year of infancy.

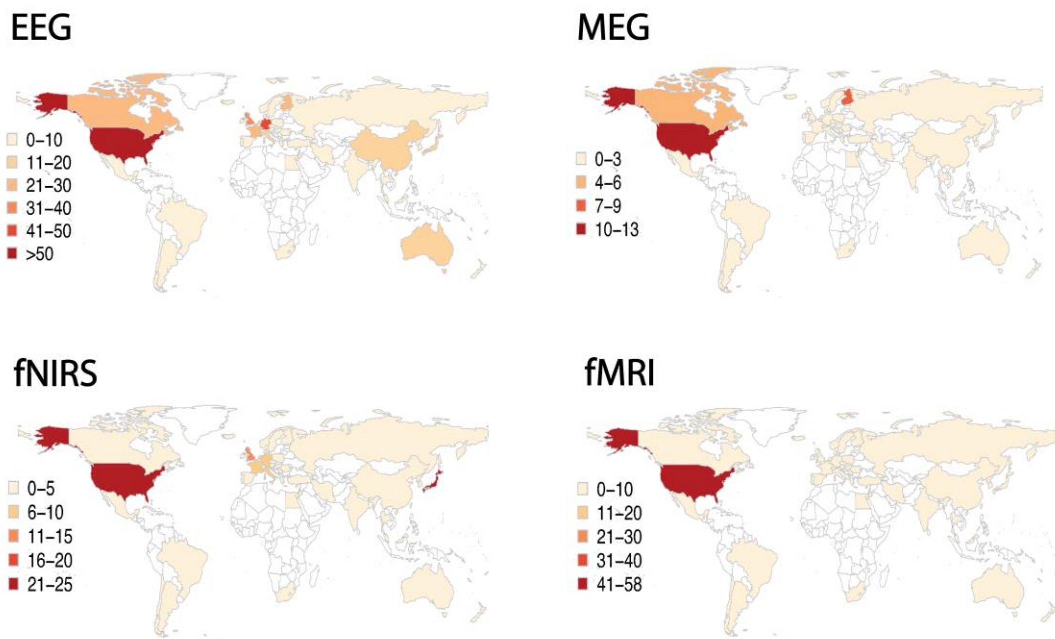

Figure 5. Geographical distribution by method. Number of infant studies using EEG, MEG, fNIRS and fMRI in different regions of the world map.

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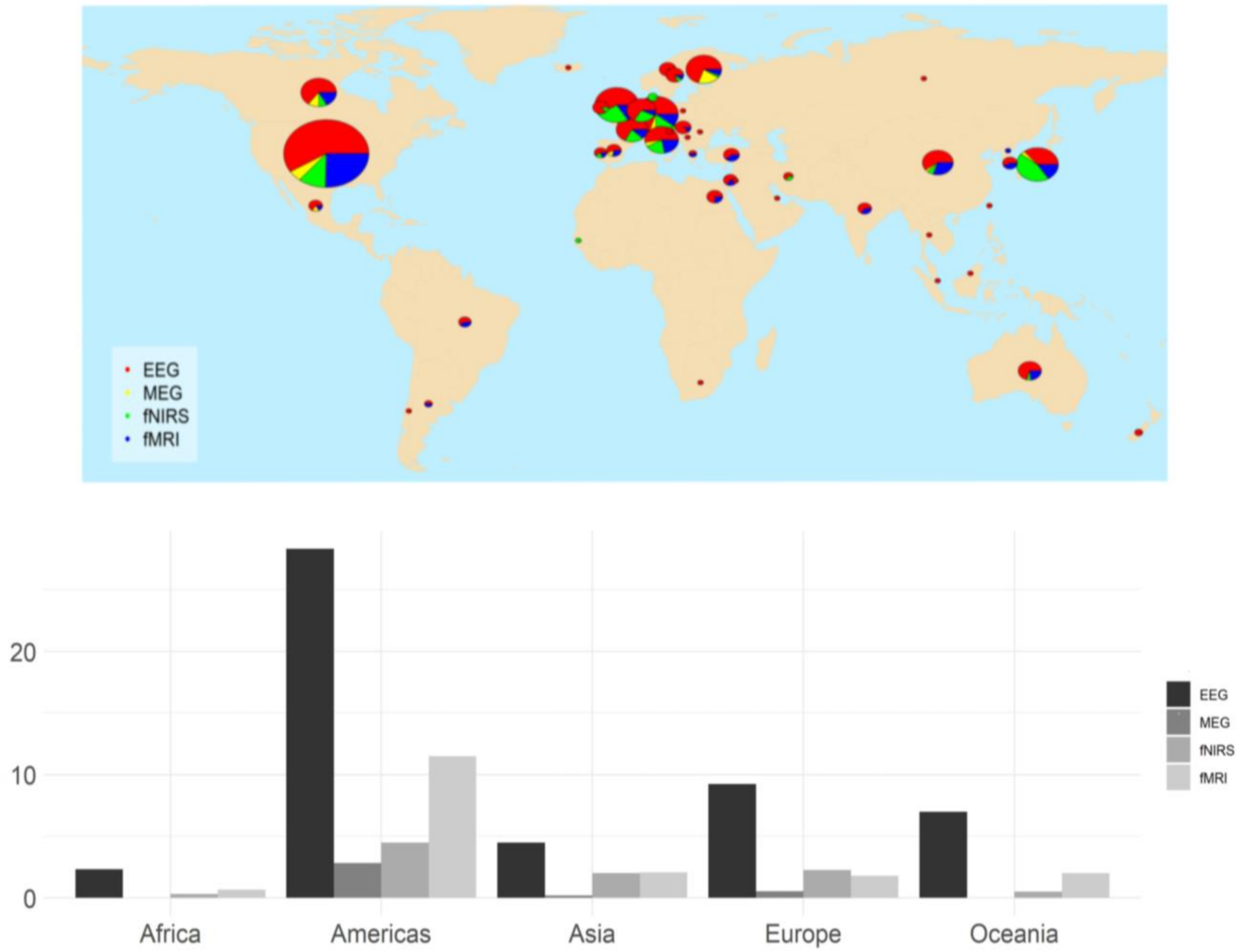

Figure 6. Distribution by method and region. a) Geo-pie plots depicting proportion of neuroimaging studies by method in each country (top), and **b)** Bar plots showing number of studies using EEG, MEG, fNIRS and fMRI in each continent (bottom).

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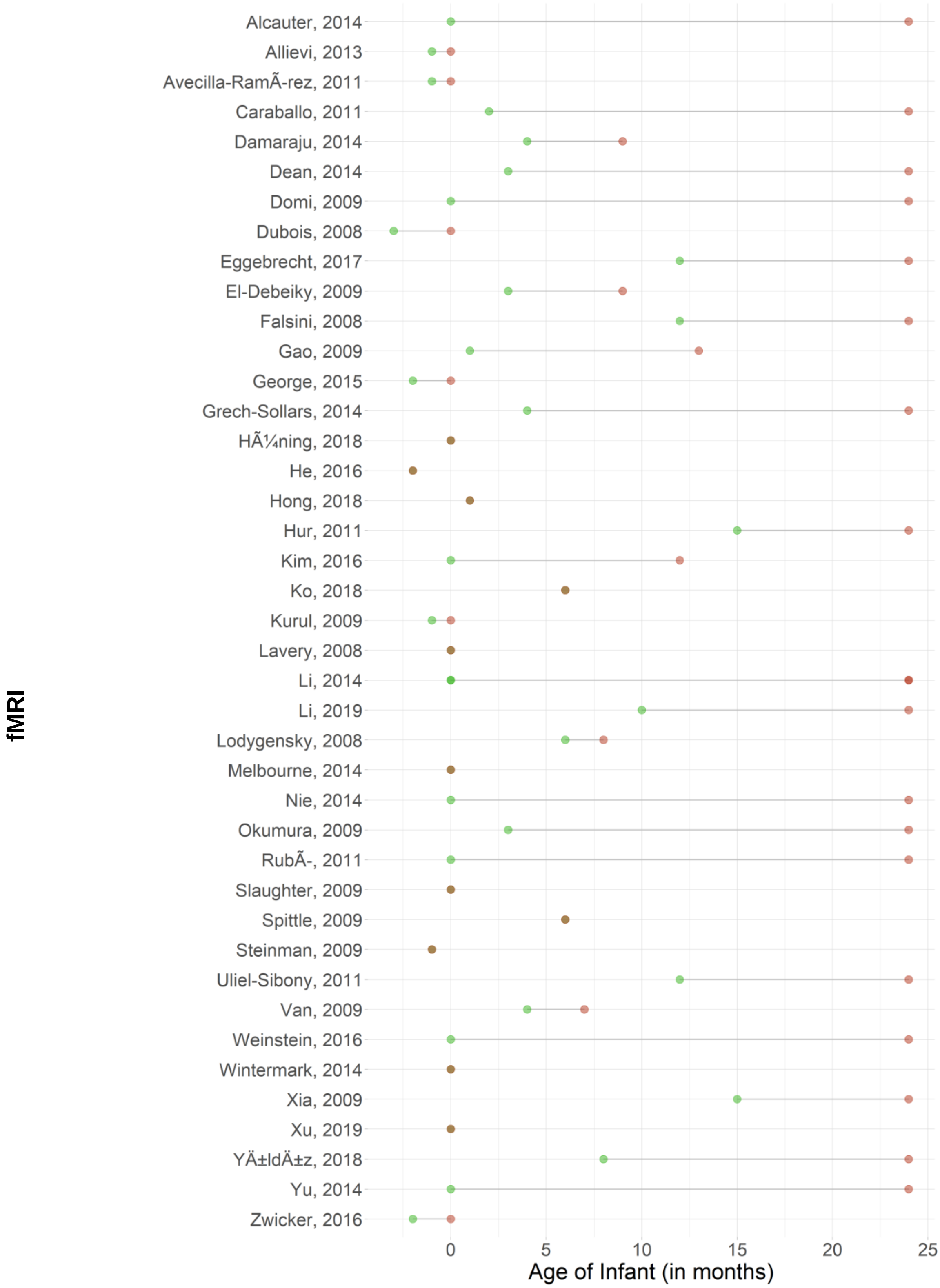

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Figure 8. Longitudinal studies by method. Lollipop plots depicting age range of infants in longitudinal studies using EEG, fNIRS and fMRI. *Note:* The same start and end age indicates that the duration between the first and second point of data collection is less than a month.

6. Perspective and Recommendations

6.1 Trend across years: Surge in EEG and fNIRS studies

The distribution plot of neuroimaging methods across the past ten years depicts a recent increase in EEG and fNIRS studies since 2017, and a decline in fMRI studies since 2014. This trend might be due to greater access to recently established supporting software for EEG and fNIRS methods (https://www.hitachihightech.com/global/about/news/2016/nr20160224.html).

It might also reflect a shift in focus of infant brain research toward investigating brain development in social interactional contexts (e.g. experiments involving naturalistic interactions) which favours the use of more portable imaging devices. Since the infant brain is especially sensitive to external influences of the surrounding social environment, this trajectory of infant brain research promises to discover new frontiers in this field.

6.2 Age of infants: Missing periods of development

The plots of infant age suggest that understanding neurodevelopment in infancy lacks crucial transitional information from the first to second years of life. Our concept of "milestones" might propel sampling of chronological periods of infancy, but crucial patterns of development remain unstudied as a result. While we have mastered the stages of behavioural development in infancy and are able to identify observable milestones such as gross motor, fine motor, cognitive and socio-emotional progress spanning from 0 to 5 years (Bornstein, Putnick, Park, Suwalsky, & Haynes, 2017), information on neurodevelopmental changes remain scarce and limited to common chronological milestones. For example, behavioural charts in the first year of infancy offer distinct developmental "red flags" or delays to look out for at specific windows marked at birth, 2, 4, 6, 9, 12, 18 and 24 months, but no certain understanding of the neurodevelopmental processes that accompany the observations at these timestamps have been identified (Dosman, Andrews, & Goulden, 2012). Thus, it is also important that imaging studies include developmental transitions at other ages (e.g. 9 months) or at times of onset of developmental events (e.g., language acquisition, walking, mirror self-recognition).

6.3 Geographical Distribution: Missing Infant Populations

Understanding the geographical distribution of neuroimaging methods for infant studies lends insight into the socio-cultural contexts from which samples have been drawn, and findings have been made, in the extant literature. World maps of geographical distribution reveal that most of our understanding of infant neurodevelopment is based on data from North America. The concentrated occurrence of infant neuroimaging studies in this single region limits the extent to which we can extrapolate findings to infant development in different socio-cultural contexts in other parts of the world (Tomlinson, Bornstein, Marlow, & Swartz, 2014). For instance, data from Africa, certain parts of Southeast Asia, South America, and Europe remain scarce, and underrepresentation of these regions restricts our understanding of how variations in cultural norms as well as parenting beliefs and practices shape infant development. Finally, the dearth of investigation in regions with poverty suggests how little we know of the ramifications of privation on infant brain and behavior. Investigation in these regions will push the boundaries of the presumed applicability of current knowledge to infant development in diverse environmental contexts.

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7. Conclusion: What Next?

We have arrived at an exciting era of infant research that uses neuroimaging techniques to investigate infant brain development in ways that were previously thought to be unattainable. However, we have not fully capitalised on these advances. In this perspective review, we draw attention to knowledge that we have yet to acquire from infants across a greater swath of developmental periods and from under- and less-developed populations. Empirical methods can be further improved by increasing sample size and utilizing several imaging methods in concert, capitalizing on their respective strengths and overcoming their respective weaknesses. Addressing these points will show the direction of infant neuroimaging studies in the coming decade.

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