AGE-RELATED DIFFERENCES IN APERIODIC MEG ACTIVITY IN CHILDREN AND ADULTS

Helmiina Ryödi
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Department of Psychology
University of Jyväskylä
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JYVÄSKYLÄN YLIOPISTO
Department of psychology

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Supervisor: Tiina Parviainen
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ABSTRACT

The equilibrium between excitation and inhibition, commonly referred to as E/I balance, in the cerebral cortex is prerequisite for normal brain functioning. Alterations in the E/I balance have been identified in various neuropsychiatric disorders, underscoring the significance of its thorough examination. At the same time developmental variations in the E/I balance are a part of the normal maturation of the brain. However, there is a lack of well-validated methods for measuring E/I balance in humans. A novel approach to assess E/I balance is 1/f aperiodic activity which bases on computational models and can be derived from EEG or MEG data. It has been suggested that particularly the slope of the spectrum, aperiodic exponent, may indicate the level of E/I balance at the neuronal population level at the cortex. While there have been some studies investigating developmental trajectory of aperiodic activity over few recent years, only limited research has used MEG or focused on possible differences between brain regions or hemispheres. The aim of this study is to examine whether the level of inhibitory and excitatory activity in the cortex, measured by aperiodic activity, differs between younger children, older children and adults in different brain regions and hemispheres.

The participants included in the study were categorized into three age groups: younger children aged 6-9, older children aged 10-14 and adults. The data consisted of MEG recordings of resting state with eyes closed. Aperiodic activity was indexed with exponent and offset. According to the results, both aperiodic parameters were lower in the adult group compared to the child groups, aligning with previous research on the developmental trajectory of aperiodic activity with age. Aperiodic activity also exhibited hemispheric differences, both parameters being smaller in the right hemisphere compared to the left. Furthermore, aperiodic activity was also reduced in the frontal lobe compared to the occipital lobe.

Regarding the E/I balance, the result of the age-related differences in the exponent would refer to higher excitation in adults compared to child groups. This indication may however partially conflict with a general perspective on brain development. The association between aperiodic activity and the E/I balance depends on numerous mechanisms, detailed exploration of which requires further research, particularly in integrating aperiodic activity and pharmacology. This study confirms the importance of considering factors such as age or developmental stage, hemisphere and brain region when assessing the level of E/I balance with aperiodic activity. Consequently, additional research is required before utilizing aperiodic activity for assessing E/I balance in clinical applications.

Keywords: aperiodic activity, E/I balance, magnetoencephalography (MEG)

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TIIVISTELMÄ

Inhibition ja eksitaation tasapaino eli E/I-balanssi aivokuorella on edellytys aivojen normaalille toiminnalle. E/I balanssin on kuitenkin todettu muuntuneen monissa eri neuropsykiatrisissa häiriöissä, minkä vuoksi sen tutkiminen on tärkeää. Samalla vaihtelu E/I-balanssissa liittyy myös aivojen normaaliin iänmukaiseen kehitykseen. E/I-balanssin mittaamiseen ihmisillä ei kuitenkaan ole olemassa selkeitä validoituja keinoja. Yksi uusi lähestymistapa on laskennalliseen malliin perustuva 1/f epäjaksollinen aktiivisuus, joka voidaan laskea EEG- tai MEG-datasta. On ehdotettu, että erityisesti epäjaksollisen aktiivisuuden spektrin kulmakerroin kertoisi E/I-balanssista aivokuorella neuronaalisten populaatioiden tasolla. Epäjaksollisen aktiivisuuden kehitystä iän myötä on tutkittu viime vuosien aikana jonkin verran, mutta tutkimusta MEG:lla ja eri aivoalueilla ja -puoliskoilla on niukasti. Tämän Pro Gradu -tutkielman tarkoituksena oli selvittää, eroaako inhibitorisen ja eksitatorisen aktiivisuuden taso aivokuorella nuorempien ja vanhempien lasten sekä aikuisten välillä epäjaksollisella aktiivisuudella mitattuna eri aivoalueilla ja -puoliskoilla.

Tähän tutkimukseen sisällytetty aineisto jaettiin kolmeen ikäryhmään, jotka olivat 6–9 –vuotiaat nuoremmat lapset, 10-14 –vuotiaat vanhemmat lapset sekä aikuiset. Tutkimukseen sisällytetty data koostui aivojen lepotila MEG-mittauksista silmät suljettuina. Epäjaksollista aktiivisuutta mitattiin kulmakerroin sekä ”offset” -parametreilla. Tulosten mukaan epäjaksolliset parametrit olivat pienemmät aikuisten ryhmässä kuin lapsiryhmissä, mikä on linjassa aikaisempien tutkimusten kanssa epäjaksollisen aktiivisuuden kehityksestä iän myötä. Epäjaksollinen aktiivisuus myös erosi aivopuoliskojen välillä niin, että se oli pienempää oikeassa kuin vasemmassa aivopuoliskossa. Lisäksi se oli pienempää frontaalialueella kuin okkipitaalialueella.

E/I-balanssin osalta tulos ikäryhmien välisistä eroista viittaisi kulmakertoimen perusteella korkeampaan eksitaatioon aikuisilla verrattuna lapsiryhmiin, mikä saattaa olla osittain ristiriitaista aivojen yleisen kehityksen näkökulmasta. Epäjaksollisen aktiivisuuden yhteys E/I-balanssiin on kuitenkin riippuvainen monista mekanismeista, joiden tarkempi kartoittaminen vaatii lisää tutkimusta erityisesti yhdistäen epäjaksollisen aktiivisuuden ja farmakologian. Tämä tutkimus vahvistaa, että erityisesti ikä tai kehityksellinen tila, aivopuolisko sekä -alue täytyy huomioida arvioitaessa E/I-balanssin tasoa epäjaksollisen aktiivisuuden avulla. Lisää tutkimusta tarvitaan, ennen kuin epäjaksollista aktiivisuutta voitaisiin hyödyntää E/I-balanssin mittaamiseen kliinisessä käytössä.

Avainsanat: epäjaksollinen aktiivisuus, E/I-balanssi, magnetoenkefalografia (MEG)

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1. INTRODUCTION

The brain is capable of adaptive changes by reshaping its structure and functions following a brain damage. Reorganization of neocortical circuits is not only induced in response to injury, but also during learning, when new skills are acquired. Development of the brain involves periods of heightened plasticity, critical periods, which enable the construction and consolidation of functional and structural networks, and therefore foster learning. Understanding the role of plasticity during the maturation of cerebral cortex offers valuable information about the influence of environmental stimuli on the neural networks, since plasticity is the fundamental resource for modulation of the brain on the basis of behavioural experience. The development of cerebral cortex is associated with asynchronous maturation of excitatory glutamatergic and inhibitory GABAergic neurons. Based on years of research, it has been discovered, that the development of GABAergic circuits is protracted relative to the development of glutamatergic circuits. This means that synaptic inhibition matures later than excitatory transmission which may be associated with the timing of critical periods in childhood (Jiang et al., 2005).

Inhibitory and excitatory inputs form a balance on a global network level which is crucial for the efficiency of cortical information processing, such as the maintenance of working memory (Sohal & Rubenstein, 2019). It is also essential for neuronal homeostasis and the formation of neural oscillations (Gao et al., 2017). However, activity dependent changes in E/I ratio are believed to enhance the plasticity which has been observed via topographic map reorganization, and therefore also enable learning (Jones, 1993). Measuring E/I balance in vivo is challenging and basically only limited to invasive methods including pharmacological or optogenetic manipulations, intra or extracellular recordings (Gao et al., 2017). There are certain imaging methods, such as PET, MRS and TMS which are able to provide information about the E/I balance in humans. These methods all enable great spatial accuracy but usually at the cost of poor temporal resolution, and they only cover single cells or local circuit levels, not global networks (Ahmad et al., 2022). Therefore, research on E/I balance is mainly limited to mice and can not be straightly generalized into human brain.

However, computational models have provided a novel proxy marker for E/I balance which is the aperiodic signal of the power spectrum, 1/f component. 1/f refers to the nature of all signals according to which power decreases exponentially when frequency increases (Donoghue, Haller, et al., 2020). Gao et al. (2017) developed a model according to which E/I balance can be estimated from a spectrum of electrophysiological recordings which represent inhibitory (GABA) and

excitatory (AMPA) currents. They also discovered that reduced inhibition is related to flattened slopes by pharmacologically altering E/I ratio.

The purpose of this thesis is to examine the possible age-related differences in E/I balance assessed with aperiodic activity when considering children and adults, measured in resting MEG. Since earlier results concerning the age–related differences in aperiodic activity are mainly limited to EEG studies and certain frequency bands, the present study aims to fill the gap in this area. Moreover, this study aims to explore the possible differences in the development of aperiodic component regarding brain regions and hemispheres. This can provide further information about the nature of 1/f aperiodic activity, whether it refers to more local or global phenomenon of the cerebral cortex.

1.1 Maturation of inhibitory and excitatory systems and the role of cortical plasticity in the development

Activity–dependent neuronal plasticity takes place in cortical circuits causing changes in synaptic connections and is therefore a prerequisite of learning and memory. Short-term memory is associated with strengthening and weakening of synapses (Mayford et al., 2012), and long-term memory on the other hand is enabled by structural reorganization of networks together with formation and loss of synapses (Bailey & Kandel, 1993). At the neurobiological level synaptic plasticity can be divided into two forms of which long-term potentiation (LTP) refers to the repeated activation of both pre- and postsynaptic neurons producing strengthening of synaptic input of the stimulated connections (Bliss & Lømo, 1973). Long-term depression (LTD) on the other hand refers to the decrease in synaptic efficacy (Spriggs et al., 2017).

Based on decades of research on brain development, it is generally known that the developing brain is more responsive to experiences than fully mature brain which means that the same experiences induce qualitatively different synaptic changes at different ages (Sperry, 1968). Research has shown that cortical plasticity, especially LTD-like motor cortical plasticity, decreases along aging and is highest during childhood (Freitas et al., 2011). Similar results have been observed regarding LTP plasticity: the study of Spriggs et al. (2017) discovered that there was a higher threshold for induction of LTP-like enhancements measured as visual evoked potentials (VEPS) in older adults.

Reduced plasticity may be due to the increased GABAergic inhibition during aging. GABAergic intracortical inhibition has been associated to activity-dependent and long-term plasticity effects in cat M1 studies. According to Ziemann et al. (1996), high GABAergic inhibition leads to less synaptic plasticity, and low GABAergic inhibition to high synaptic plasticity in animals but there is only few research conducted in humans. Walther et al. (2009) showed that intracortical inhibition was lower in children compared to adults and also lower in adolescents than in adults after paired-pulse transcranial magnetic stimulation (TMS). Also McGinley et al. (2010) observed similar findings about older adults exhibiting more intracortical inhibition and less intracortical facilitation than younger adults. These results suggest that the maturation process of GABAergic intracortical inhibition is present in humans as well. A possible explanation for increased intracortical inhibition may be multiplication of $GABA_A$ receptors during human brain maturation as shown by Brooks-Kayal & Pritchett (1993).

GABAergic neurons are mainly interneurons which function as depolarizing at the beginning but later turn as hyperpolarizing (Xing et al., 2021). This change in GABAergic transmission from excitatory to inhibitory leads to the maturation of GABAergic system. The development of GABAergic circuitry does not only begin earlier than the maturation of excitatory glutamatergic system, but it is also much slower process. Rodent studies indicate that the slow maturation is crucial in the timing of cortical plasticity, especially during critical periods (Pouille & Scanziani, 2001). Research has shown that GABAergic inhibition may also be responsible for the onset and termination of the critical periods. As GABAergic circuits mature later than glutamatergic system, the strength of inhibition needs to get on a certain “permissive” level for critical period to begin (Jiang et al., 2005). According to Jiang et al. (2005), critical period also continues until the upper threshold of that range is crossed. This implies that inhibition increases until it reaches a certain point again which determines that critical period is finished. In this case, it may indicate that the level of maturation of GABAergic system would also determine the duration of critical period. The role of inhibition in closure of critical period is however still under debate, but the needed mismatch in the level of inhibition and excitation for the period of activity-dependent plasticity to occur, seems clear.

1.2 E/I balance

As described, the level of cortical excitatory and inhibitory inputs is initially mismatched due to the slow maturation of GABAergic circuitry. This is a part of the normal developmental variation of the balance between excitation and inhibition, E/I balance, which is crucial for the proper cortical circuit function. At a single neuron level it also enables precise and effective information processing. The exact definitions of E/I balance differ in literature. E/I balance can be defined either on a single cell or global circuit level, and also the temporal window over which synaptic currents are summed in the measurement varies, since there is no clear definition of the time frame (He & Cline, 2019). According to He & Cline (2019), temporal windows used in the literature may vary from only several to hundreds of milliseconds. This problem concerning refinement of the time frame usually concerns cell recordings.

At the network level, E/I balance however generally reflects a stable global level of activity in a certain circuit, regardless of the fact that individual neurons might display certain dynamic imbalances (Sohal & Rubenstein, 2019). Previously discussed plasticity mechanisms, LTD and LTP, can alter the strengths of excitatory and inhibitory synapses and therefore cause temporary fluctuations in the E/I balance (Field et al., 2020). For example activity-dependent changes in external input may produce some short-term alterations in the balance which are considered to promote the circuit plasticity by topographic map reorganization (Jones, 1993). According to Lamsa et al. (2005) long-term plasticity increasing the strength of excitation relative to inhibition also extends the window for spike integration. Bartley & Dobrunz (2015) found that this also concerns short-term plasticity: it regulates E/I ratio and temporal window for spike integration. While there is a general tendency for excitatory and inhibitory inputs to be balanced, the level of the E/I balance can vary dynamically due to the network activity, plasticity mechanisms, homeostatic regulation, and developmental stage (Field et al., 2020). This dynamic characteristic of the E/I balance allows brain to adapt to changing conditions and optimize information processing while maintaining network stability.

Main principle in the maintenance of E/I balance is based on the regulation of the excitatory and inhibitory systems. Structural properties of neocortex involve elemental units of signal processing, minicolumns, which are narrow radial arrays of neurons (Tatti et al., 2017). Excitatory activity of pyramidal neurons within a minicolumn is balanced by different types of inhibitory neurons, such as PV interneurons and chandelier cells (Tatti et al., 2017). Therefore, strength of synaptic connections between neurons in minicolumns enable establishment of balanced activity between

inhibition and excitation, making possible concurrent processing of incoming signals. However, it is not completely understood, how the neural circuits are adjusted to establish the balance. At the single cell level, it has been described that factors such as intrinsic neuronal excitability (He & Cline, 2019) contribute to the establishment of the balance. At the circuit level, in addition to the complex interaction between inhibitory and excitatory systems, also circuit formation and excitability of the network have been suggested to contribute (Culotta & Penzes, 2020).

Alterations in the balance of excitation and inhibition have been observed in many neuropsychiatric disorders. As some alterations towards more excitation may at some level foster neuroplasticity, on the other hand more stable changes in the balance are considered to underlie the pathology of neuropsychological conditions and disorders, such as autism spectrum disorder (ASD) (Gonçalves et al., 2017; Rubenstein & Merzenich, 2003; Sohal & Rubenstein, 2019), schizophrenia (Chance et al., 2008), ADHD (Mamiya et al., 2021) and Fragile X Syndrome (Wilkinson & Nelson, 2021). Findings are however somewhat contradictory – for example results regarding ASD have found both increased (Rubenstein & Merzenich, 2003) and decreased (Gonçalves et al., 2017) E/I ratio. Gonçalves et al. (2017) even suggested that the nature of changes may be dependent on the brain region. Alterations in the balance have been generally linked to dysfunctions in the minicolumn functioning (Chance et al., 2008; Tatti et al., 2017) which is crucial for the balanced activity between inhibitory and excitatory systems and concurrent signal processing.

Studies examining E/I balance in the context of neuropsychiatric disorders have, however, used various methods to define and measure the E/I balance, which may explain the incoherence in the results. Alterations in the E/I balance could potentially serve as a possible biomarker in diagnostics of various psychiatric disorders in clinical settings in the future, but further research is needed. Most importantly, a common validated method to assess E/I ratio reliably and noninvasively in humans is required, also to clarify the non-pathological developmental trajectory of E/I balance.

1.2.1 Markers of E/I balance in human neuroscience

Most of the research connecting neurodevelopmental conditions and alterations in the E/I balance has however been conducted using animal models. Measuring E/I balance in humans is challenging and would generally require invasive methods such as optogenic techniques, pharmacological manipulations, extracellular recordings and intracellular clamp recordings (Ahmad et al., 2022). Most of these methods are also limited to measure E/I balance on a single cell level which means

that the results can not necessarily be generalized into global networks. Methods such as MRS, PET and TMS are able to cover local populations and regions across the brain and also enable spatial accuracy but on the other hand lack temporal resolution (Gao et al., 2017). Considering these limitations, it is clear that there is a need for new methods of assessing E/I balance reliably.

Previous literature has linked beta and gamma power and frequencies to the interplay of excitatory glutamatergic cells and inhibitory GABAergic interneurons. According to pyramidal interneuron network gamma (PING) model, PV interneurons and excitatory pyramidal neurons cause synchronized rhythmic activity through delayed feedback inhibition of PV interneurons (Tada et al., 2020). The auditory steady-state response (ASSR) has been used to detect alterations in gamma band activity, which requires appropriate regulation of inhibition to excitation (Tada et al., 2020), and of which PV interneurons are mainly responsible. Therefore, it has been considered as a marker of PV interneuron functioning and E/I balance. Nevertheless, many studies have proved no connections between GABA levels, gamma power and gamma frequency (Cousijn et al., 2014). Gamma rhythms have also been prevalent in neural regions which do not have local E/I connections (Jenkinson et al., 2013). This is inconsistent considering that pyramidal cell activity is responsible for generating gamma oscillations. Beta oscillations on the other hand are linked to the function of inhibitory interneurons and modulated by GABA (Ahmad et al., 2022).

It. has been suggested that modulation of gamma and beta power by pharmacological manipulations may be due to a shift in frequency and related up or downregulation of oscillations in a separate frequency band (Ahmad et al., 2022). These conventional traditional markers for E/I ratio alone however do not offer a valid unambiguous method for assessing E/I balance which is why recent studies have proposed aperiodic activity to explain alterations in the E/I balance. Before covering the role of aperiodic activity as a possible proxy marker for the balance of excitation and inhibition, I will first specify how the changes in rhythmic activity are exhibited in the development.

1.3 Periodic activity and maturational changes

Periodic activity, including previously introduced gamma and beta oscillations, is induced by the rhythmic fluctuations in the excitability of neurons and by shifts in the E/I balance. Oscillatory activity has been researched for decades and it is also linked to a wide range of cognitive functions, behavioral states and developmental processes (Kahana, 2006). Oscillations are sensitive to

maturational changes which include different structural and functional processes related to the neurological development, such as differentiation and specialization of cortical circuits, axonal pruning and changes in the E/I connections (Hill et al., 2022). The main trend observed in the developmental trajectory of neural oscillations is the decrease of activity within lower frequency ranges, delta and theta oscillations, and the increase of high frequency power, especially within the alpha and beta bands, as the brain matures (Clarke et al., 2001; Cragg et al., 2011; Gómez et al., 2013; Ott et al., 2021). Hunt et al. (2019) have also found that changes in the oscillations related to age were actually dependent on the region – alpha increasing with age in the temporal area and gamma increasing with age in the frontal lobe.

Concerning the maturation of brain regions, Katada et al. (1981) found that the age-related changes in oscillation development first took place in the occipital regions which was followed afterwards by the posterior and frontal regions. Also, the study of Clarke et al. (2001) observed that changes occur first and faster in posterior regions where they are also larger than in frontal regions. Besides the development of regions, also hemispheres have been observed to develop at different pace. Parviainen et al. (2019) discovered that in 7–8-year-old children right hemisphere of the auditory cortex showed more mature signs of activity than the left hemisphere. These results are consistent with the general development of the brain, and it is therefore crucial to examine the impact of the brain region and hemisphere also in the context of the development of aperiodic activity which will be introduced in the following.

1.4 Aperiodic activity as a marker of human brain signaling

Alongside the oscillations, EEG and MEG signal also consists of non-oscillatory aperiodic activity which has previously gained rather limited attention in the literature. Most of the studies related to the changes of oscillatory power in certain narrowbands do not consider that the change in the power can also be due to the changes in the aperiodic component. Aperiodic signal follows a 1/f distribution which refers to the power decreasing exponentially as the frequency increases (Donoghue, Haller, et al., 2020). The aperiodic activity consists of two parameters, an exponent (slope) and an offset which both have been linked to the integration of underlying synaptic currents (Voytek, 2015). Exponent determines the steepness of the 1/f like decay and offset refers to the shift of power across frequencies in the broadband (Donoghue, Haller, et al., 2020). Offset has also been considered to reflect neuronal population spiking activity (Voytek et al., 2015).

The literature has previously referred to aperiodic component as a noise, but recent studies have now begun to recognize the actual functional and physiological significance of the signal. Aperiodic activity has been proven to change by task performance (He et al. 2010), arousal levels (Lendner et al., 2020) and pharmacological drugs (Waschke et al., 2021). Alterations in the aperiodic activity have also been observed in different neurological and psychiatric conditions, such as autism spectrum disorder (Manyukhina et al., 2022). Gao et al. (2017) have developed a computational model according to which aperiodic activity is also linked to the balance between excitation and inhibition. Model enables estimation of the E/I balance from the exponent parameter of the power spectrum, and it was tested by varying E/I ratio pharmacologically with rats and measuring the effect on the slope. The results showed that reducing inhibition pharmacologically was correlated with flattening of the slope in the frequency range of 30-70hZ. According to Donoghue et al. (2020), this is due to the fact that power of excitatory currents is relatively constant at lower frequencies before rapidly decaying whereas within inhibitory GABA currents power decays more slowly.

Aperiodic component can be computed by a FOOOF algorithm introduced by Donoghue et al. (2020) which parameterizes power spectral densities (PSDs) from EEG and MEG data and extracts them into periodic and aperiodic components. Method does not require the defining of canonical narrow bands of oscillation frequencies, and instead identifies oscillations based on their power over and above the aperiodic activity. Evidence linking E/I balance and aperiodic exponent indicates that aperiodic exponent measured in human EEG and MEG can provide a promising noninvasive marker for the global population level E/I ratio (Ahmad et al., 2022) but further research is still required.

1.4.1 Previous research related to the development of aperiodic activity across lifespan

Literature has shown that imbalances in E/I ratio underlie many neuropsychiatric conditions, and these results have also been showed by altered aperiodic activity. In order to comprehensively understand the neuropathologies behind these disorders and to consider aperiodic activity as a possible biomarker for E/I balance, it is crucial to understand how the cortical maturation of the brain and age influences the behavior of aperiodic activity. Research on the effects of age and brain maturation on the aperiodic component has only begun during the recent few years.

So far, several studies have indicated that the main trend in the development of the aperiodic activity would be the decrease of the signal with age, usually referring to both exponent and offset. Less negative exponent, referring to flattened slope, and lower offset has been observed with increased age in studies comparing younger and older adult groups (Donoghue, Haller, et al., 2020; Merkin et al., 2021, 2022; Pathania et al., 2022; Voytek et al., 2015). Also research related to the development of the aperiodic activity in childhood has found similar observations regarding to the reduction of the exponent and offset, beginning early in the development (Cellier et al., 2021; Hill et al., 2022; McSweeney et al., 2021; Schaworonkow & Voytek, 2021).

According to the previously introduced model of Gao et al. (2017), previous findings would suggest an increase of excitation and a reduction of inhibition as the age increases. Considering 1/f activity being a marker for E/I balance, this seems inconsistent in a light of development of inhibitory and excitatory systems and plasticity decreasing with age. Based on what is known about the protracted maturation of GABAergic inhibition related to glutamatergic excitation and increase of intracortical inhibition with age, it could be also possible that the slope would steepen across age. Therefore, it is essential to thoroughly examine the behaviour of the aperiodic activity in different age groups, frequency ranges and brain regions before drawing stronger conclusions.

1.5 Aims of the study

The purpose of this study was to examine whether the level of the balance of inhibitory and excitatory activity at cortex differs between adults and children. This was measured by aperiodic activity in resting MEG, at eyes closed condition. Regardless of the previous results suggesting increased aperiodic values and therefore increased excitation with age, studies conducted so far have used solely EEG and rather limited frequency band. The result of smaller exponent values (flatter slope) with age is also controversial based on what is known about the role of the development of inhibitory and excitatory systems and the cortical brain development in general. Since the previous research has not examined aperiodic activity in different brain regions or the role of the hemispheres, the aim of this study is additionally explore, whether age-related differences in aperiodic activity show different pattern in the two hemispheres and brain regions using MEG.

Regardless of the similar capabilities for temporal resolution of both EEG and MEG, the advantage of MEG in measuring developmental differences in resting data is the good signal localization ability (Hämäläinen et al., 1993). Besides, EEG is more vulnerable for changes in

cortical thickness in the development at various ages which impair the signal quality (Candelaria-Cook et al., 2022). Due to its precise signal localization, MEG also enables reliable examination of the differences within brain regions. The brain regions included in the study, frontal and occipital lobes, were selected based on their distinct timing of maturation. According to Taki & Kawashima (2012), gray matter density peaks first in the occipital lobe, progressing last to the frontal lobe. This refers to faster maturation of occipital lobe as compared with frontal lobe which could also be observable in aperiodic activity. Taken these aspects into consideration, research questions include:

1. Do the aperiodic parameters exponent, suggested to reflect E/I balance, and offset differ between adults, older children and younger children?
2. Do the aperiodic parameters exponent and offset differ by brain region and hemisphere?
3. Do the differences between age groups in aperiodic parameters offset and exponent vary depending on region or hemisphere?

Based on the previous research on the development of the aperiodic activity across lifespan, it is expected that the results would refer to smaller exponent and lower offset in adult than child groups, and that older children also have smaller exponent and lower offset than younger children. However, since the frequency range used in this study differs from the previous ones, it may be also possible, that the results show different pattern as well. Grounding on the earlier observations of the occipital lobe showing patterns of earlier maturation than the frontal lobe (Clarke et al., 2001; Katada et al., 1981) and the right hemisphere showing more mature signs of activity in children than the left hemisphere (Parviainen et al., 2019), it is also expected that the aperiodic component is smaller in occipital area and in right hemisphere than in frontal area and left hemisphere.

2. METHODS

The present study uses data collected in the research project Signatures of auditory processing development (van Bijnen et al., 2022). In the project MEG data was recorded during rest and three different auditory tasks. Tasks consisted of a passive listening task, an auditory Go/No-go task, and an auditory oddball task which were all executed in a context of a game in a visual environment. Resting state recordings were performed prior to the tasks and they were conducted two times for both eyes closed and eyes open conditions alternately, approximately 1.5 minutes per condition. The data included in this thesis involves resting state MEG recordings of children and adults of the first eyes closed condition, since the second one was recorded last and involved more disturbance related to the opening of eyes and other problems concerning concentration of the children.

2.1 Participants

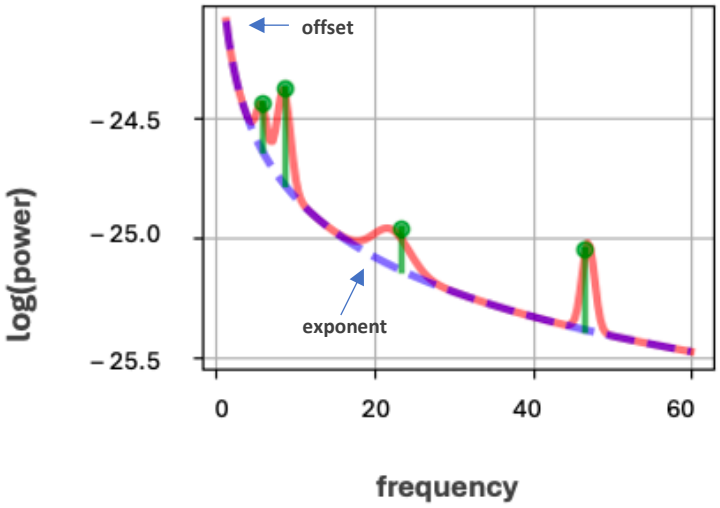
Participants included 67 children and 16 adults who were recruited from schools and the National Registry. Also email-lists and notice boards were used. All participants had normal hearing which was assessed with an audiometer. They had no neurological disorders or medication which could affect the central nervous system. Children were aged between 6 and 14 (M=10.2 years, SD=1.4) and 36 of them were boys and 31 girls. Adults (13 women, 3 men) included in the study were 20–30 years old (M=24.8, SD=3.4). All the participants, and additionally also parents of children, gave an informed consent for the study which had also gained approval by the Ethics Committee of the University of Jyväskylä. Participants were also given a compensation (either a movie ticket or a gift card) for participating. For the purposes of the present study participants were divided into three groups: children under 10 years old (n=32), children over 10 years old (n=35) and adults (n=16).

2.2 MEG data analysis

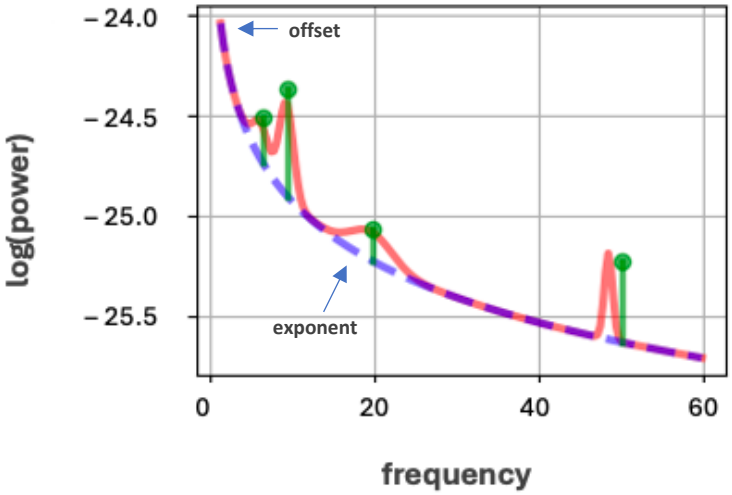
Resting data was recorded with a 306-channel MEG system (Elekta Neuromag® TRIUXTM, MEGIN Oy, Helsinki, Finland). Raw MEG data was first filtered for removing of external noise using MaxFilter program which removes interfering signals originating from sources outside the head. After performing the noise removal, MEG data was processed with the Meggie program (Heinilä & Parviainen, 2022). ICA (independent component analysis) method was used to remove artifacts caused by eye blinks or movements and heartbeat from the data. Two periods with eyes open and eyes closed were recorded, resulting in four blocks of MEG data. While performing spectral analysis, data was thus separated into four time intervals individually for every participant according to the conditions. Duration of the four blocks varied slightly between participants but lasted approximately for 1,5 minutes per condition. Only first eyes closed condition was included in the statistical analysis, since the second one involved more disturbances from eye-opening and concentration issues in children. Spectrums were created with the overlap of 512 and the length of window being 1024.

After performing the spectral analysis, the FOOOF toolbox was used to extract aperiodic component from the periodic signal using frequency range from 1 Hz to 60 Hz. This range was chosen since most of the previous research have limited the range to 40 Hz which may exclude some information of the higher frequencies. Fitting was done with 'fixed' mode since there was not a clear 'knee' in the power spectrum when the output was visually inspected. Other spectral parameterization settings were peak width low = 0.50 Hz, peak width high = 12.00 Hz, peak threshold (relative) = 2.00, minimum frequency = 1.30 Hz, maximum frequency = 59.90 and maximum number of peaks = 6. Final outputs included exponent and offset values of both hemispheres of frontal and occipital lobes and goodness of fit measures for the FOOOF algorithm performance which were used to evaluate the validity of the modeling. Example spectrums of the FOOOF model fit are presented in the figure 1.

a)



b)



c)

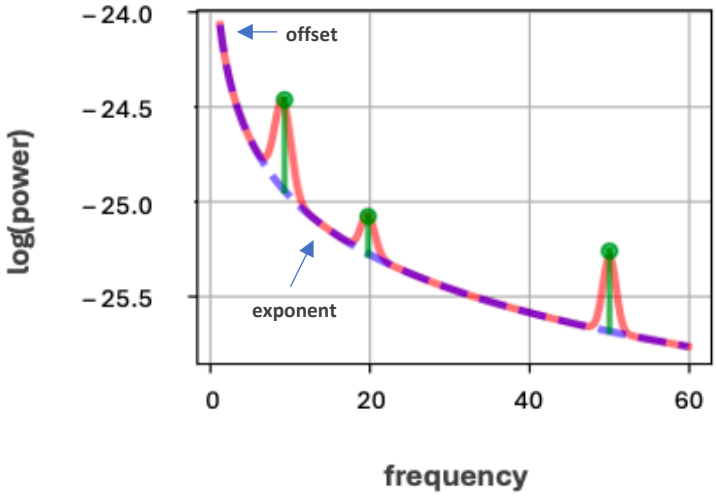


FIGURE 1. Example spectrums of the FOOOF model fit from a single participants in the left frontal lobe in age groups of a) under 10 year olds, b) over 10 year olds and c) adults

2.3 Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics, version 26. Two extreme outliers in the variable offset were detected and interpreted from boxplots. Extreme outliers were brought close to the normal distribution's tail by giving new values to outliers which still retained the correct order of the participants' values. The assumption of normality of the sample was then tested with the Kolmogorov-Smirnov and Shapiro-Wilk tests which proved the assumption fulfilled in both variables. The effect of age group (research question 1), the effect of hemisphere and brain region (research question 2) and their possible interaction (research question 3) were tested by using repeated measures of ANOVA. This was performed separately for both dependent variables, offset and exponent. Within-subject factors were brain region (frontal/occipital) and hemisphere (left/right) whereas age group (adults/old children/young children) was a between-subjects factor. Pairwise post hoc comparisons using Bonferroni correction were performed if main effects were found. Association between age and both aperiodic parameters was also tested separately for children and adults using Pearson's correlation across the four brain regions. Fit of the FOOOF algorithm is also reported with the goodness of fit measures of the model, R2 and error.

3. RESULTS

There was a significant main effect of the group on both exponent ($F(2, 80) = 26.70$, $p < .001$, $np^2 = .400$) and offset ($F(2, 80) = 19.16$, $p < .001$, $np^2 = .324$), meaning that exponent and offset values values varied depending on the age group. Pairwise post hoc analyses using Bonferroni correction revealed that offset was significantly lower in adult group ($M = –23.647$, $SE = .060$) compared to both younger ($M = –23.192$, $SE = .043$, $p < .001$) and older ($M = –23.329$, $SE = .041$, $p < .001$) child groups. The results were similar regarding exponent which was significantly smaller in adult group ($M = .968$, $SE = .035$) than in younger ($M = 1.274$, $SE = .024$, $p < .001$) and older ($M = 1.202$, $SE = .023$, $p < .001$) child groups. Child groups did not differ from each other in either offset ($p = .066$) or exponent ($p <.106$).

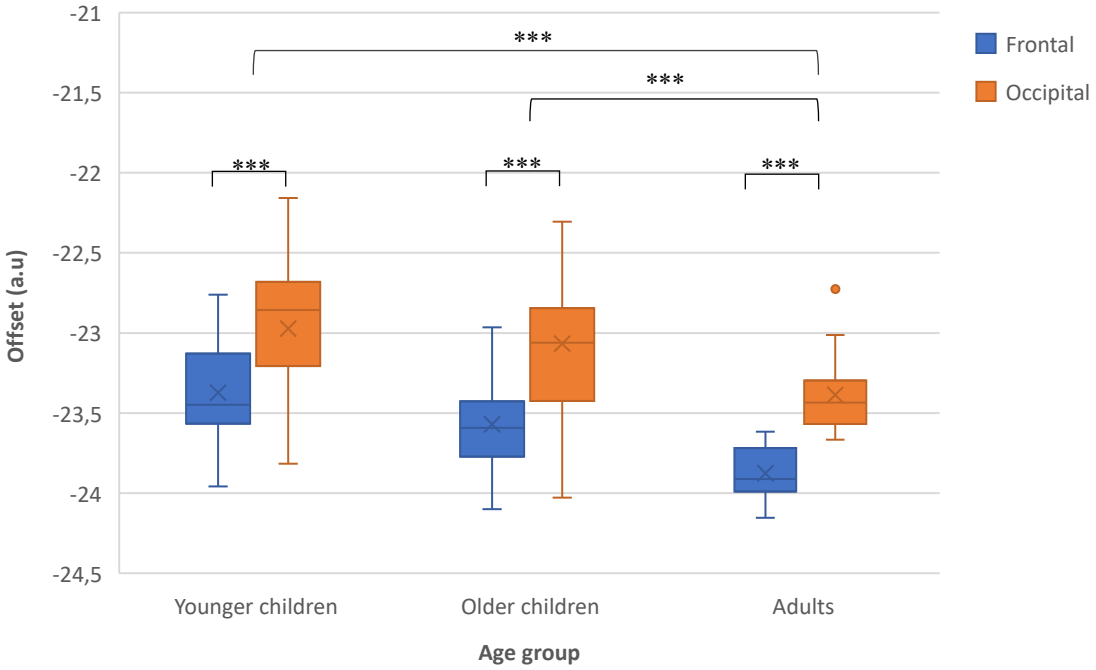
There was also a significant main effect of the brain region on exponent ($F(1,80) = 56.479$, $p < .001$, $np^2 = .414$) and offset ($F(1,80) = 71.856$, $p < .001$, $np^2 = .473$). Pairwise post hoc tests indicated that exponent was smaller in the frontal ($M = 1.070$, $SE = .021$) than in the occipital lobe ($M = 1.226$, $SE = .021$). This was also the case with offset; it was smaller in the frontal ($M = –23.622$, $SE = .030$) than in the occipital lobe ($M = –23.156$, $SE = .046$). Significant difference was also observed on the effect of hemisphere again on both exponent ($F(1, 80) = 4.214$, $p = .043$, $np^2 = .050$) and offset ($F(1, 80) = 6.166$, $p = .015$, $np^2 = .072$). Post hoc analyses revealed that exponent was smaller in the right hemisphere ($M = 1.142$, $SE = .016$) than in the left hemisphere ($M = 1.154$, $SE = .016$). Results concerning the other parameter were similar; offset was smaller in the right hemisphere ($M = –23.405$, $SE = .028$) than in the left ($M = –23.405$, $SE = .029$).

Regarding offset, there was no interaction effects found between age group and region ($F(2, 80) = .265$, $p = .768$, $np^2 = .007$), age group and hemisphere ($F(2, 80) = .223$, $p < .800$, $np^2 = .006$) or age group, brain region and hemisphere together ($F(2, 80) = 1.301$, $p < .278$, $np^2 = .032$). These results indicate that offset did not significantly change in hemispheres or brain regions differently based on the age group. Results were similar in exponent, no two way or three way interactions were found between age group and brain region ($F(2, 80) = .642$, $p < .529$, $np^2 = .016$), age group and hemisphere ($F(2, 80) = .947$, $p < .392$, $np^2 = .023$) or age group, brain region and hemisphere ($F(2, 80) = 1.090$, $p < .341$, $np^2 = .027$). Differences in aperiodic activity between age groups, brain regions and hemispheres are presented in the figure 2.

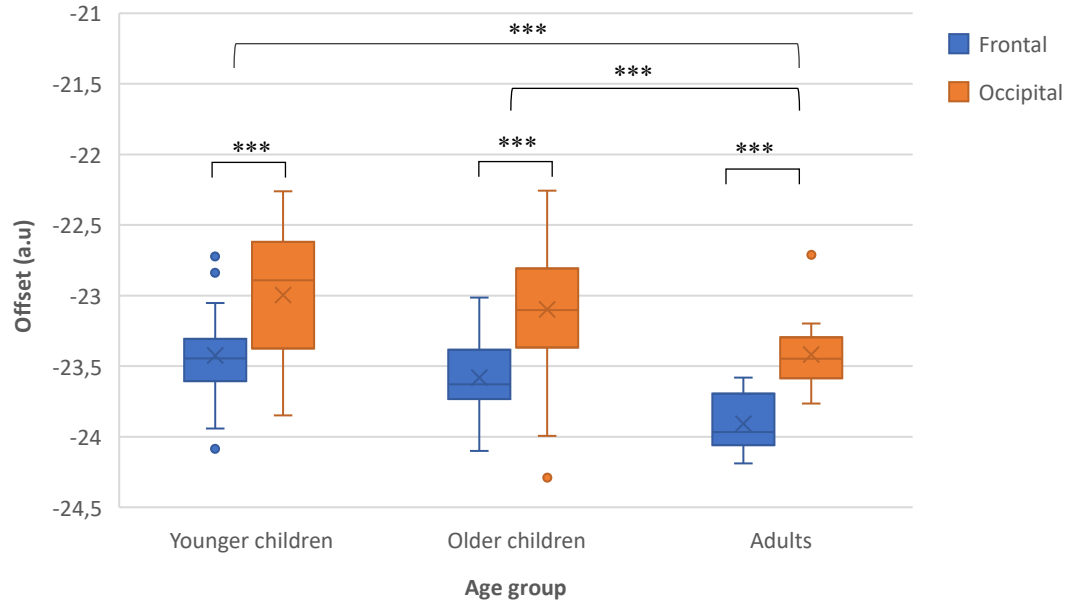
Goodness of fit metrics of the algorithm were assessed averagely for all participants. R^2 values were all found to be high and the error values low, and the results were similar across all of the four

brain regions and the age groups (R^2 = .98, Error = .05). This suggests that the model fits the data well. The descriptive statistics of the aperiodic components in all age groups are presented in the appendices.

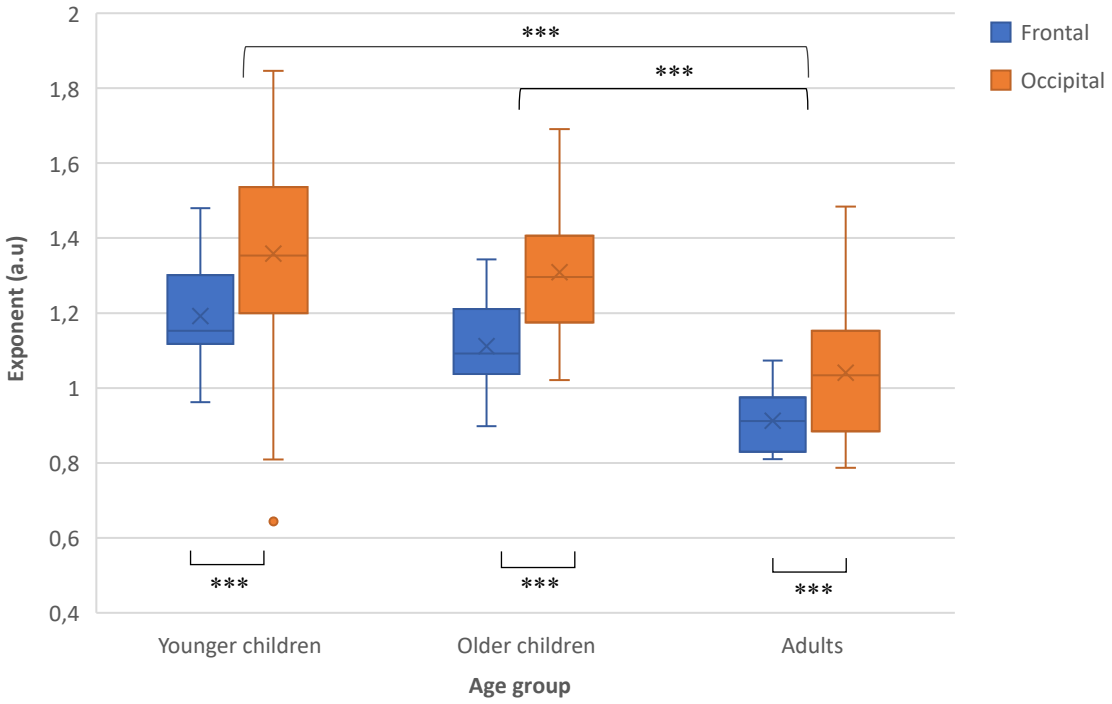
a) left offset



b) right offset



c) left exponent



d) right exponent

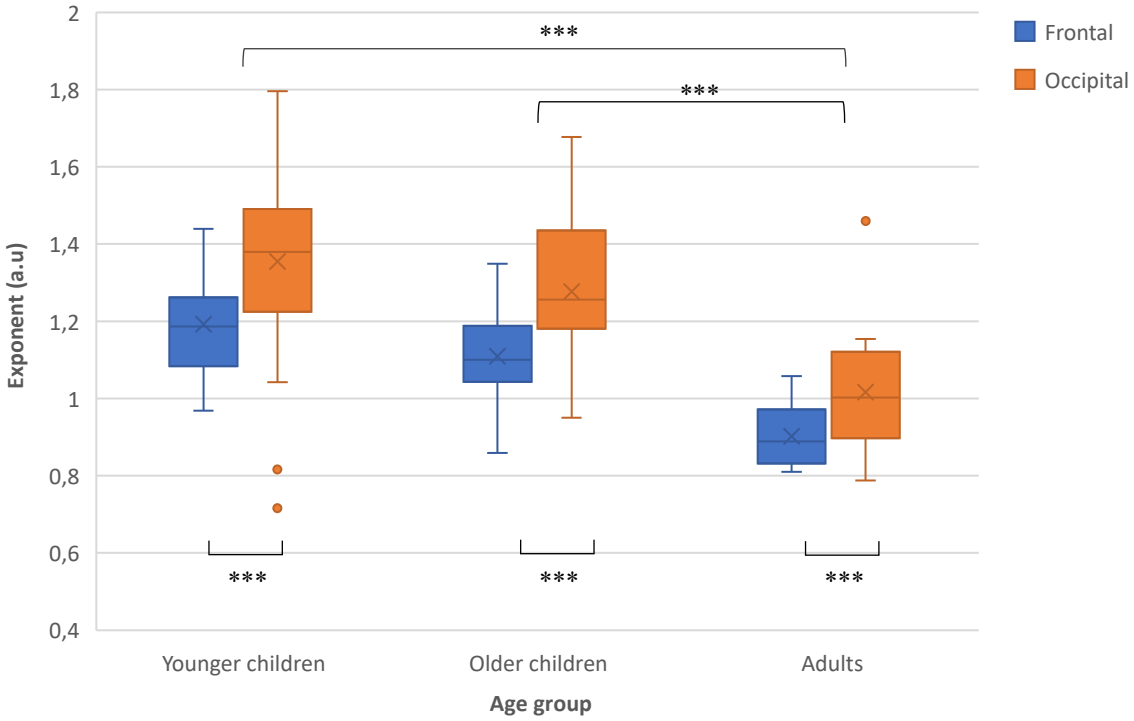


FIGURE 2. Differences in aperiodic activity between the age groups and the brain regions in a) left offset, b) right offset, c) left exponent and d) right exponent. *** $p < .001$

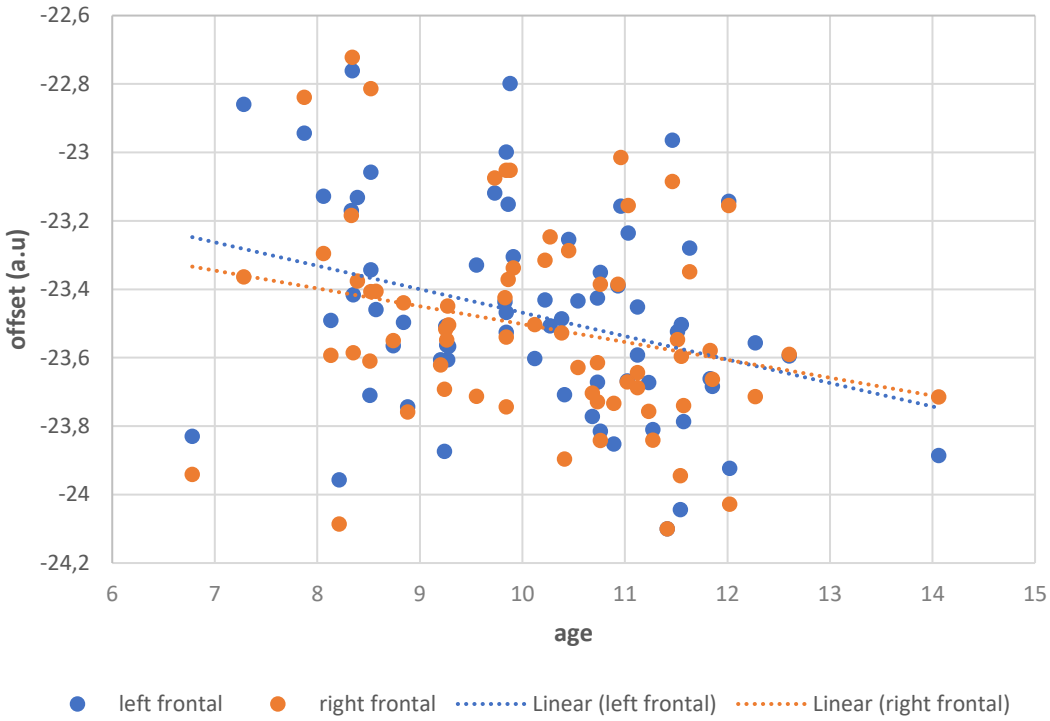
Correlations between age and exponent in children were significant both in left frontal (r = –.342, p = .005) and the right frontal lobe (r = –.291 = .017) but not in the left or the right occipital lobe. Also offset was similarly negatively correlated with age in children both in the left frontal (r = –.324, p = .007) and the right frontal lobe (r = –.252, p = .040) but again not in the left or the right occipital lobe. In adults, age did not correlate with either exponent or offset in any of the four brain regions. All the correlations are documented in the table 1 and the significant ones are additionally presented in the figure 3.

TABLE 1. Pearson's correlations between age and aperiodic component in children and adults.

	left frontal	right frontal	left occipital	right occipital
exponent children	–.342 **	–.291 *	–.186	–.201
offset children	–.324 **	–.252 *	–.147	–.133
exponent adults	–.097	–.066	.160	.280
offset adults	–.156	–.148	.098	.214

*Note. * p < .05, ** p < .01, *** p < .001*

a)



b)

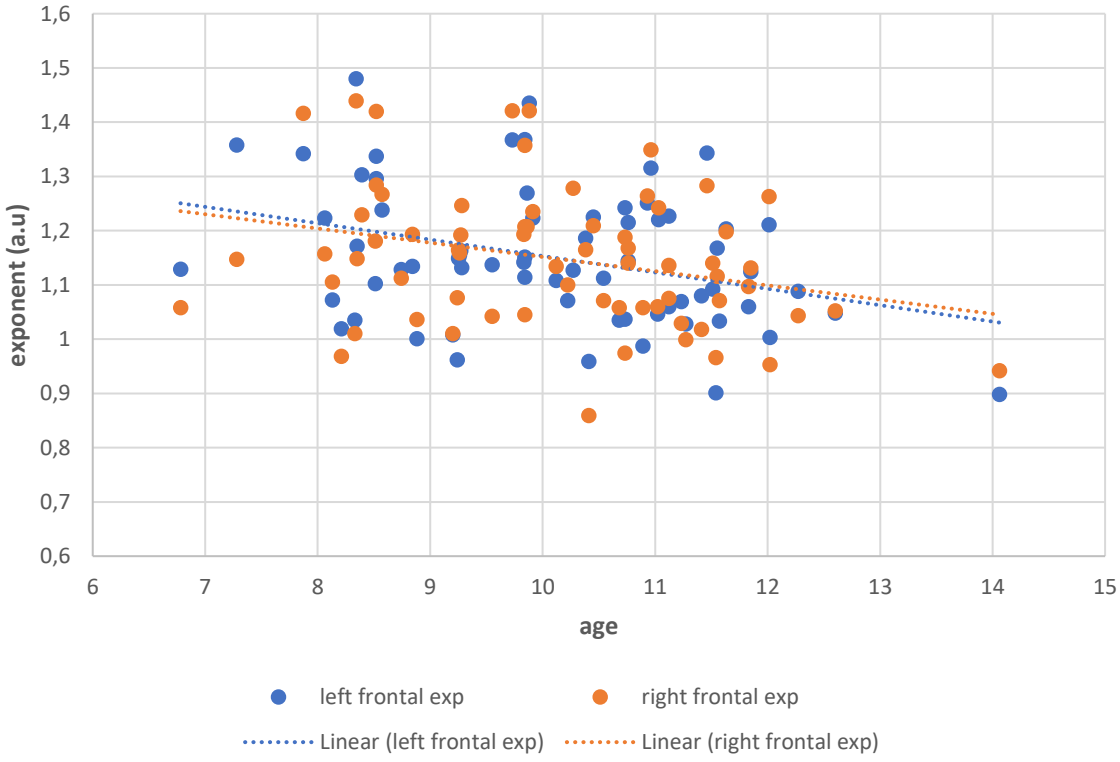


FIGURE 3. Scatter plots of the significant correlations between a) offset and age in children, and b) exponent and age in children

4. DISCUSSION

The aim of this study was to examine the development of E/I balance assessed with aperiodic activity by comparing the offset and exponent parameters within three age groups consisting of younger children, older children and adults. Moreover, this study also aimed to clarify the possible differences in the aperiodic activity related to the brain region and hemisphere. Additionally, the final purpose was to find out, whether the possible differences in the aperiodic activity differ in age groups depending on region or hemisphere. Both offset and exponent were smaller in the adult group than in child groups which partly supports the hypothesis of aperiodic component decreasing with age, which in turn would refer to increased excitation with age. Child groups did not differ from each other, although difference approached significance. The results regarding the hemisphere showed that both offset and exponent were decreased in right hemisphere in comparison to left hemisphere as was hypothesized. Aperiodic activity also differed between brain regions, offset and exponent both being smaller in frontal than in occipital areas which was not supported by the hypothesis according to the which the exponent would be smaller in the occipital than in the frontal lobe.

4.1 Differences in aperiodic activity across age groups

The result of smaller exponent and offset in adults as compared with child groups is mainly in line with the previous results suggesting that the aperiodic component decreases with age, referring especially to the slope flattening along the maturation. Using EEG, the study of Donoghue et al. (2020) has observed findings related to flatter slope and reduced offset in adults compared to children in frequency range of 1–40 hZ. Measured with MEG, the study of He et al. (2019) found comparable findings indicating the reduction of offset and flattening of slope in adults compared to children, in participants aged between 8-12- and 41–47-year-old. Flattening the of the slope and reduction of offset with age has also been observed in adult groups of different age: Donoghue et al. (2020), Pathania et al. (2022) and Merkin et al. (2021) all showed that aperiodic signal was more decreased in older than younger adults. However, there are only few studies which have included elderly. The study of Brady & Bardouille (2022) showed that aperiodic activity decreased until the age of 60, but subsequently began to increase, eventually returning to the initial level.

Correlational analyses showed that age did not correlate with the measures of aperiodic activity in adults. The group consisted of 16 adults which is relatively small number for reliably assessing correlation, which may have impacted the results. The age range in the adult group was also quite small and most of the adults were aged between 20–25 years. It also needs to be considered that if aperiodic activity is a trait like feature, there is a lot of individual variation in the levels of GABA and glutamate which may have also impacted the results.

Aperiodic activity of children groups in the current study did not differ from each other which basing on the exponent, would suggest that the E/I balance is similar in these age groups. However, the difference in exponent was nearly significant, older children having tendency of flatter slope which according to Gao et al. (2017), would again refer to increased excitation. Results of the aperiodic activity not differing in these age groups may also be explained by the small age gap between the groups. Original sample was not recruited with the aim of comparing two different child groups but as a single sample of children age varying around 10 years. This leads most of the children in age group 10–14 being 10–12-year-olds and the group of 6–9-year-olds including mainly 8–9-year-olds.

Interestingly, children showed correlation between age and both aperiodic parameters, exponent and offset, in the frontal regions but not in the occipital regions. This result partly supports the age-related flattening of the slope and reduction of the offset with age. Previous results have also shown that reduction in offset and flattening of the slope across age is also present in children in different ages. Cellier et al. (2021) found that aperiodic signal decreased along the maturation across the ages of 3–24 in the frequency range of 1-40hZ. Hill et al. (2022) observed similar results in children aged 4-12 years old and Schaworonkow & Voytek (2021) even in infants aged 38–203 days. Results of the present study suggest that such age-related reduction appears more clearly in frontal regions in children aged 6–14.

Majority of the previous studies suggest the reduction of aperiodic exponent with age and therefore the increase of excitation related to inhibition. However, there are also contradictory results concerning the development of the E/I balance in adolescence. Larsen et al. (2022) conducted an fMRI-based model which was applied to examine the GABA modulated functional connectivity in adolescence. The results showed that E/I ratio reduced in the association cortex between the ages of 12.9 and 16.7. This suggested that the inhibition was increased during this period which was related to the opening of the critical period. This may also explain the result of aperiodic activity not differing between child groups, since the age group of 10-14 year-olds overlaps the period of adolescence and the time of possible changes related to the critical period. McSweeney et al. (2021) on the other hand conducted a longitudinal EEG study of the development

of aperiodic activity between the ages of 13 and 15 and found that the slope was however flattened with age also during this period of time.

The general practice is to examine both aperiodic parameters together. However, exponent and offset differ in their considered functional significance and neural mechanisms. As exponent is associated to E/I balance, it can also refer to increased synchronous neural background firing which is regulated by E/I ratio (Voytek et al., 2015). According to Voytek et al. (2015) flattening of the slope was also associated with cognitive decline in a working memory task when comparing younger and older adults. Offset on the other hand reflects the shifts in the broadband power which are positively correlated with neuronal spiking (Manning et al., 2009). Therefore, reduced offset with age suggests a maturational decline in the rate at which cortical neurons fire.

4.2 Differences in aperiodic activity in regions and hemispheres

Regarding the second research question about the differences in aperiodic activity in hemispheres and brain regions, the results showed that exponent was flatter and offset smaller in right hemisphere and in frontal area than in left hemisphere and occipital area. The results of the flatter slope and reduced exponent in the right related to left hemisphere was in line with the hypothesis. This observation may suggest that the maturation of the left hemisphere is protracted related to the right. So far, studies which have examined the hemispheric differences related to the aperiodic activity are lacking. Only Brady & Bardouille (2022) observed that aperiodic exponent was smaller in left hemisphere compared to the right which is contradictory to the result of the present study. No hemispheric differences in offset were found (Brady & Bardouille, 2022). The study of Parviainen et al. (2019) however observed stronger and more mature activity in right than left hemisphere on the auditory cortex which suggested faster maturation of the right hemisphere compared to the left. Also the study of Bosch-Bayard et al. (2022) observed predominance of the right hemisphere in the EEG connectivity between various regions during the first three years. Chi et al. (1977) have discovered that right hemisphere also develops first in the ontogenetic development of the brain. Based on aforementioned findings, the result of the flatter slope and reduced offset in right hemisphere may refer to the earlier maturation related to the left hemisphere. However, the result of the present study must be interpreted with caution, since also contradictory findings exist. Further research on hemispheric differences is needed to establish the maturational development of aperiodic activity.

Concerning the aperiodic differences between brain regions, results showed that both aperiodic parameters slope and offset were smaller in frontal than in occipital regions. This is contradictory to the hypothesis stated and the previous observations suggesting that the age-related changes in oscillation development occur earlier in the occipital than the frontal regions (Katada et al., 1981). Also Clarke et al. (2001) observed similar findings of oscillatory changes occurring first, faster and as larger in the posterior than the frontal regions. However, Hunt et al. (2019) suggested that age-related oscillatory spontaneous activity is dependent on the region and found that gamma increased with age primarily in the frontal lobe in the sample consisting of 6–45-year-olds. Furthermore, Ott et al. (2021) observed that increase in gamma and decrease in delta with age occurred in frontal areas. They also found that increase in beta with age occurred in occipital, parietal and temporal areas of which the occipital lobe was the strongest. These results are relevant considering the frequency range 1-60hZ used in the present study, which also includes low gamma frequencies. Since the decrease in offset represents the shift of power from lower frequencies more to higher frequencies, it may therefore explain the smaller values in frontal than in occipital area at least in the aperiodic offset. Therefore, it is possible that the differences of the aperiodic activity between the regions may be dependent on the age-related changes in oscillatory power. Age correlated with aperiodic activity in children in both frontal areas but not in occipital regions which may also be explained by the increase in gamma in frontal areas. However, it must be strongly noted that previous results on regional differences are limited to oscillation development which can not be straightly generalized into the development of aperiodic activity. Therefore, the result of the present study, of aperiodic parameters being smaller in frontal than occipital regions, requires further examination.

Regarding the third research question, this study also aimed to examine whether the possible variation in aperiodic activity differed in age groups depending on the region and hemisphere. There was no interaction between hemisphere and age group or brain region and age group, pointing out that differences in aperiodic activity between all the age groups were similar in both hemispheres and both brain regions. This means that the effect of age was similar in both left and right hemisphere, and both in frontal and occipital lobe. The differences in aperiodic activity between left and right hemisphere were also similar in both frontal and occipital area, and vice versa. These results are in line with the hypothesis according to which the differences in aperiodic activity in age groups were expected to be similar across the brain. Since the age-related differences in the groups appeared similarly in both regions and hemispheres, these results suggest that aperiodic activity seems to be a stable global trait of the cortex and also displays similarly throughout the cortex. This is supported by Cellier et al. (2021) who also found that there were no

interaction effects between age and brain region (frontal-midline and parietal-midline) on exponent and offset measured in EEG. Nevertheless, in the present study correlational analyses showed that age was associated with both aperiodic parameters in children, in frontal but not in occipital regions, which is partly contradictory considering that no interactions between age group and brain region were found. This may imply that the effect of age may have been too subtle to induce any significant changes between the groups or that the age group division may have been somewhat factitious. Therefore, it may be also possible that the correlational analyses reveal the actual result better than the division into the groups with Anova.

4.3 1/f aperiodic activity across age: The role as a biomarker for E/I balance?

The present study suggests that aperiodic exponent is decreased in adults compared to children which based on the study of Gao et al. (2017), would refer to increased excitation with age. In the light of what is known about the general development of inhibition increasing with age, it can be questioned, whether aperiodic activity truly captures the phenomenon of E/I balance. The original connection of decreased exponent across age and increased excitation related to inhibition is based on the study of Gao et al. (2017) in which the direction of aperiodic exponent was tested through pharmacological manipulation. Propofol which is known to affect on $GABA_A$ receptors and increase inhibition, steepened the exponent. This correlation was further confirmed by Waschke et al. (2019) who compared propofol with ketamine, which is known to increase excitation. The findings indicated that ketamine flattened the slope. However, it needs to be noted that Gao et al. (2017) used the frequency range of 30-70 hZ which excludes the lower frequencies and differs from the majority of studies examining aperiodic activity. Waschke et al. (2019) on the other hand fitted the spectra into the frequency range of 2–60hZ which is consistent with the present study and strengthens the role of aperiodic activity as a promising biomarker for E/I balance.

Furthermore, studies examining aperiodic activity in the context of unconscious and consious states have found that exponent was lower in NREM sleep (Lendner et al., 2020) and anesthesia (Colombo et al., 2019) than awake states. Conscious states are generally linked to increased excitation, and unconscious states on the other hand are associated with increased inhibition. These results therefore also seem to provide support for the lowered aperiodic exponent indicating increased excitation in the E/I balance. However, in contrast to the results of increased E/I ratio with age, Legon et al. (2016) examined glutamatergic and GABAergic connections and found that older

adults had higher inhibitory tone and lower excitatory tone (lower E/I ratio) than the younger adults when measured with dynamic causal modeling (DCM) for fMRI. They also showed that GABAergic connectivity was higher in aged than younger group, measured with DCM.

In general, the earlier studies examining the development of GABA across age have found conflicting results, with some reporting increases and others reporting decreases in cortical GABA. Porges et al. (2021) conducted a study in which 8 datasets were integrated into a model of the development of frontal GABA across whole lifespan, measured with MRS. They found that trajectory of GABA involves a developmental period of increase which is followed by a stabilization phase in early adulthood and then a gradual decrease with aging. There are also reports on older age being associated with lower GABA levels on cortex (e.g. Gao et al., 2013). According to Maes et al. (2018), age-related variations in GABA levels are though at least partly due on cortical gray matter loss rather than changes in GABA levels. Nevertheless, Hermans et al. (2018) and Lissemore et al. (2018) have reported lower GABAergic inhibition in older compared to younger adults which is therefore in line with the findings of Brady & Bardouille (2022) related to the increase in aperiodic activity after the age of 60.

These conflicting results on the developmental changes in GABA concentration seem to underline the need for a better establishment of the neural mechanisms underlying E/I balance and the developmental trajectory of both GABA and glutamate. GABA functions primarily through two receptor subtypes which are ionotropic $GABA_A$ receptors and metabotropic $GABA_B$ receptors, which both have distinct roles in the neurotransmission (Allen et al., 2024). $GABA_A$ receptors are ligand-gated chloride channels which are responsible for fast synaptic inhibition. $GABA_B$ receptors are G-coupled protein receptors and function through later and slower synaptic transmission. Besides the early depolarization of GABA in the brain development, it has been suggested that GABAergic depolarization and excitation may be present in various regions also in the mature brain (Marty & Llano, 2005). Also Chavas & Marty (2003) have discovered that inhibitory and excitatory GABA synapses coexist in cerebellar interneuron network. According to Marty & Llano (2005), these excitatory functions can be divided to phasic excitatory effects by $GABA_A$ receptor activation and sustained excitatory effects which refers to prolonged activation of $GABA_A$ receptors. In certain cortical interneurons reversal potential (E_{GABA}) is more depolarized than in pyramidal cells which leads to excitatory effects of GABAergic afferent stimulation. Minor alterations in intracellular chloride and potassium concentrations are able to switch the sign of the effects (Marty & Llano, 2005)

Thus, GABAergic synapses exhibit a higher level of adaptability also in mature brain than previously assumed which may also affect the interpretation of the E/I balance. However, based on

the findings of the present and previous studies of the decreased aperiodic activity in a light of the results of Waschke et al. (2018) connecting aperiodic exponent to E/I ratio, it seems that aperiodic activity may function as a valid and promising marker for E/I balance.

4.4 Limitations and strengths of the present study

Limitations of the study include relatively low number of adults which weakens the reliability of the results concerning adults. The adult group also consisted of relatively young participants, and the variation of age may have been too small to induce changes in the correlation analyses. Ages of children in the two groups may have also been too close to each other for differences to appear, since the recruitment of the children was targeted mainly on 8–12-year-olds. Consequently, the age ranges in the groups were notably close to each other. Furthermore, the group of older children included also 13–14-year-olds. Given the earlier results indicating alterations in E/I balance occurring during the critical periods in adolescence (Larsen et al., 2021), individuals within this age range may have impacted the results.

The choice of the frequency range can be considered both as a limitation but on the other hand also as a strength of the present study. Majority of the studies examining the development of aperiodic activity with age have limited the frequency range to 1–45 hZ (e.g. Donoghue et al., 2020; Hill et al., 2022; Merkin et al., 2022) which is not in line with the broadbands which Gao et al. (2017) and Waschke et al. (2018) originally linked to the E/I balance. The frequency range of the present study is similar to the one in the study of Waschke et al. (2018). Due to the fractal character of the aperiodic signal, estimation of the spectral parameters should however not depend on the chosen frequency range (Donoghue, Dominguez, et al., 2020). Regardless, non-neural artefacts, including muscle activity (such as small microsaccades), are frequently observed in higher frequencies (Muthukumaraswamy, 2013), which may have biased the spectrum. FOOOF assumes that all the peaks, that represent oscillations as Gaussian functions, are within the fitting range because partial Gaussian peaks are not fitted. If peaks are overlapping partially, modeling process becomes complicated and may alter the slope (Gerster et al., 2022). In the current study, some of the PSDs seemed to have slightly overlapping peaks which means that the challenge also concerns the data of the present study.

Another limitation related to the estimation of the 1/f slope is the possible presence of the spectral plateau which lowers the exponent already at 10 hZ (Gerster et al., 2022). According to

Gerster et al. (2022), the upper fitting range is therefore recommended to be chosen as low as possible to minimize the bias. Since oscillation peaks masked the spectral plateau, detecting the onset is difficult and makes the PSD vulnerable for biasedly lowered exponent. However, given that the present study focused on the relative changes in differences between the groups, this problem may be somewhat avoided.

Correlations between the aperiodic parameters were not reported in the results section because they were not related to the research questions. Nonetheless, it should be noted that the parameters were strongly correlated which might account for the similar findings observed in both the offset and the exponent. High correlation between the parameters can be considered as a common limitation for the studies examining aperiodic activity. Regardless of the considered distinct functional significances and neural mechanisms of the parameters, according to McSweeney et al. (2021), changes in exponent magnitude may result in concomitant changes in offset as well. This unfortunately weakens the validity of the results regarding offset and makes the interpretations complicated. Moreover, Merkin et al. (2023) point out that any alteration in the 1/f structure which causes a rotation of the power spectrum around a non-zero frequency, will induce highly correlative modifications in both offset and exponent.

The use of MEG can be considered as a strength of the present study, since apart from the study of He et al. (2019), nearly all studies examining aperiodic activity are conducted on EEG. According to Muthukumaraswamy & Singh (2013), MEG is characterized by improved signal-to-noise ratio when measuring high-frequency oscillations compared to EEG. Moreover, the advantage of MEG includes more precise spatial localization compared to EEG (Hämäläinen et al., 1993), which also allowed the accurate examination of the brain regions and hemispheres in the context of aperiodic activity which has not been studied previously.

4.5 Implications and future research

The findings of the present study complement the growing literature of the age–related differences in aperiodic activity. They also provide further evidence for the decrease of aperiodic activity with age, of which the reduction of exponent may be linked to the developmental changes in E/I balance. Basing on the results regarding regional differences, this study suggests that aperiodic activity may be a general stable trait which is displayed similarly throughout the cortex. Clear understanding of the normative development of aperiodic activity at different ages and states of development would clarify the role of the brain maturation in aperiodic activity which possibly enables further use of

the exponent as an index for E/I imbalances related to neuropsychiatric disorders. Measurement of aperiodic activity with the FOOOF parameterization enables investigation of large datasets retrospectively which opens possibilities to combine data related to the development of inhibitory and excitatory mechanisms in humans.

Since aperiodic activity is still a relatively novel research topic, nearly all the studies conducted so far are cross-sectional. Given the recognized variability in aperiodic activity among individuals, future research should adopt longitudinal approaches to examine the developmental trajectory of aperiodic activity across age. Additionally, comparisons between clinical and nonclinical samples are needed to elucidate the potential role of aperiodic activity as a possible biomarker for E/I balance. In addition to age-related differences, aperiodic activity may be sensitive to other features that may impact its development, such as sex, which needs to be established thoroughly before assessing aperiodic activity as a marker of E/I balance in the context of neuropsychiatric conditions.

4.6 Conclusions

Both aperiodic parameters offset and exponent were reduced in adults compared to both children groups which referred to increased excitation related to inhibition. Aperiodic activity differed also in hemispheres, offset and exponent both being smaller in the right than the left hemisphere. Regional differences were shown as smaller exponent and decreased offset in the frontal lobe compared to the occipital lobe. Results provide support for the previous research related to the flattening of the slope with age. However, relation to the development of excitation and inhibition remains speculative and still requires further understanding of the mechanisms underlying E/I balance. Especially, further research combining pharmacological studies and aperiodic activity is needed. The present study confirms that age and developmental state need to be taken into consideration when measuring E/I balance indexed as aperiodic activity. So far, the role of the aperiodic activity as a possible formal biomarker for E/I balance requires further examination.

REFERENCES

Ahmad, J., Ellis, C., Leech, R., Voytek, B., Garces, P., Jones, E., Buitelaar, J., Loth, E., dos Santos, F. P., Amil, A. F., Verschure, P. F. M. J., Murphy, D., & McAlonan, G. (2022). From mechanisms to markers: Novel noninvasive EEG proxy markers of the neural excitation and inhibition system in humans. *Translational Psychiatry*, *12*, 467. https://doi.org/10.1038/s41398-022-02218-z

Allen, M. J., Sabir, S., & Sharma, S. (2024). GABA Receptor. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK526124/

Bailey, C. H., & Kandel, E. R. (1993). Structural Changes Accompanying Memory Storage. *Annual Review of Physiology*, *55*(1), 397–426. https://doi.org/10.1146/annurev.ph.55.030193.002145

Bartley, A. F., & Dobrunz, L. E. (2015). Short-term plasticity regulates the excitation/inhibition ratio and the temporal window for spike integration in CA1 pyramidal cells. *European Journal of Neuroscience*, *41*(11), 1402–1415. https://doi.org/10.1111/ejn.12898

Bliss, T. V. P., & Lømo, T. (1973). Long-lasting potentiation of synaptic transmission in the dentate area of the anaesthetized rabbit following stimulation of the perforant path. *The Journal of Physiology*, *232*(2), 331–356. https://doi.org/10.1113/jphysiol.1973.sp010273

Bosch-Bayard, J., Biscay, R. J., Fernandez, T., Otero, G. A., Ricardo-Garcell, J., Aubert-Vazquez, E., Evans, A. C., & Harmony, T. (2022). EEG effective connectivity during the first year of life mirrors brain synaptogenesis, myelination, and early right hemisphere predominance. *NeuroImage*, *252*, 119035. https://doi.org/10.1016/j.neuroimage.2022.119035

Brady, B., & Bardouille, T. (2022). Periodic/Aperiodic parameterization of transient oscillations (PAPTO)–Implications for healthy ageing. *NeuroImage*, *251*, 118974. https://doi.org/10.1016/j.neuroimage.2022.118974

Brooks-Kayal, A. R., & Pritchett, D. B. (1993). Developmental changes in human ?-aminobutyric acida receptor subunit composition. *Annals of Neurology*, *34*(5), 687–693. https://doi.org/10.1002/ana.410340511

Candelaria-Cook, F. T., Solis, I., Schendel, M. E., Wang, Y.-P., Wilson, T. W., Calhoun, V. D., & Stephen, J. M. (2022). Developmental trajectory of MEG resting-state oscillatory activity in children and adolescents: A longitudinal reliability study. *Cerebral Cortex*, *32*(23), 5404–5419. https://doi.org/10.1093/cercor/bhac023

Cellier, D., Riddle, J., Petersen, I., & Hwang, K. (2021). The development of theta and alpha neural oscillations from ages 3 to 24 years. *Developmental Cognitive Neuroscience*, *50*, 100969. https://doi.org/10.1016/j.dcn.2021.100969

Chance, S. A., Casanova, M. F., Switala, A. E., & Crow, T. J. (2008). Auditory cortex asymmetry, altered minicolumn spacing and absence of ageing effects in schizophrenia. *Brain*, *131*(12), 3178–3192. https://doi.org/10.1093/brain/awn211

Clarke, A. R., Barry, R. J., McCarthy, R., & Selikowitz, M. (2001). Age and sex effects in the EEG:

Development of the normal child. *Clinical Neurophysiology*, *112*(5), 806–814. https://doi.org/10.1016/S1388-2457(01)00488-6

Colombo, M. A., Napolitani, M., Boly, M., Gosseries, O., Casarotto, S., Rosanova, M., Brichant, J.-F., Boveroux, P., Rex, S., Laureys, S., Massimini, M., Chieregato, A., & Sarasso, S. (2019). The spectral exponent of the resting EEG indexes the presence of consciousness during unresponsiveness induced by propofol, xenon, and ketamine. *NeuroImage*, *189*, 631–644. https://doi.org/10.1016/j.neuroimage.2019.01.024

Cousijn, H., Haegens, S., Wallis, G., Near, J., Stokes, M. G., Harrison, P. J., & Nobre, A. C. (2014). Resting GABA and glutamate concentrations do not predict visual gamma frequency or amplitude. *Proceedings of the National Academy of Sciences*, *111*(25), 9301–9306. https://doi.org/10.1073/pnas.1321072111

Cragg, L., Kovacevic, N., McIntosh, A. R., Poulsen, C., Martinu, K., Leonard, G., & Paus, T. (2011). Maturation of EEG power spectra in early adolescence: A longitudinal study. *Developmental Science*, *14*(5), 935–943. https://doi.org/10.1111/j.1467-7687.2010.01031.x

Culotta, L., & Penzes, P. (2020). Exploring the mechanisms underlying excitation/inhibition imbalance in human iPSC-derived models of ASD. *Molecular Autism*, *11*(1), 32. https://doi.org/10.1186/s13229-020-00339-0

Donoghue, T., Dominguez, J., & Voytek, B. (2020). Electrophysiological Frequency Band Ratio Measures Conflate Periodic and Aperiodic Neural Activity. *eNeuro*, *7*(6), ENEURO.0192-20.2020. https://doi.org/10.1523/ENEURO.0192-20.2020

Donoghue, T., Haller, M., Peterson, E. J., Varma, P., Sebastian, P., Gao, R., Noto, T., Lara, A. H., Wallis, J. D., Knight, R. T., Shestyuk, A., & Voytek, B. (2020). Parameterizing neural power spectra into periodic and aperiodic components. *Nature Neuroscience*, *23*(12), Article 12. https://doi.org/10.1038/s41593-020-00744-x

Field, R. E., D'amour, J. A., Tremblay, R., Miehl, C., Rudy, B., Gjorgjieva, J., & Froemke, R. C. (2020). Heterosynaptic Plasticity Determines the Set Point for Cortical Excitatory-Inhibitory Balance. *Neuron*, *106*(5), 842-854.e4. https://doi.org/10.1016/j.neuron.2020.03.002

Freitas, C., Perez, J., Knobel, M., Tormos, J. M., Oberman, L., Eldaief, M., Bashir, S., Vernet, M., Peña-Gómez, C., & Pascual-Leone, A. (2011). Changes in Cortical Plasticity Across the Lifespan. *Frontiers in Aging Neuroscience*, *3*. https://doi.org/10.3389/fnagi.2011.00005

Gao, F., Edden, R. A. E., Li, M., Puts, N. A. J., Wang, G., Liu, C., Zhao, B., Wang, H., Bai, X., Zhao, C., Wang, X., & Barker, P. B. (2013). Edited magnetic resonance spectroscopy detects an age-related decline in brain GABA levels. *NeuroImage*, *78*, 75–82. https://doi.org/10.1016/j.neuroimage.2013.04.012

Gao, R., Peterson, E. J., & Voytek, B. (2017). Inferring synaptic excitation/inhibition balance from field potentials. *NeuroImage*, *158*, 70–78. https://doi.org/10.1016/j.neuroimage.2017.06.078

Gerster, M., Waterstraat, G., Litvak, V., Lehnertz, K., Schnitzler, A., Florin, E., Curio, G., & Nikulin, V. (2022). Separating Neural Oscillations from Aperiodic 1/f Activity: Challenges and Recommendations. *Neuroinformatics*, *20*(4), 991–1012. https://doi.org/10.1007/s12021-022-

09581-8

Gómez, C., Pérez-Macías, J. M., Poza, J., Fernández, A., & Hornero, R. (2013). Spectral changes in spontaneous MEG activity across the lifespan. *Journal of Neural Engineering*, *10*(6), 066006. https://doi.org/10.1088/1741-2560/10/6/066006

Gonçalves, J., Violante, I. R., Sereno, J., Leitão, R. A., Cai, Y., Abrunhosa, A., Silva, A. P., Silva, A. J., & Castelo-Branco, M. (2017). Testing the excitation/inhibition imbalance hypothesis in a mouse model of the autism spectrum disorder: In vivo neurospectroscopy and molecular evidence for regional phenotypes. *Molecular Autism*, *8*(1), 47. https://doi.org/10.1186/s13229-017-0166-4

Hämäläinen, M., Hari, R., Ilmoniemi, R. J., Knuutila, J., & Lounasmaa, O. V. (1993). Magnetoencephalography—Theory, instrumentation, and applications to noninvasive studies of the working human brain. *Reviews of Modern Physics*, *65*(2), 413–497. https://doi.org/10.1103/RevModPhys.65.413

He, H., & Cline, H. T. (2019). What Is Excitation/Inhibition and How Is It Regulated? A Case of the Elephant and the Wisemen. *Journal of Experimental Neuroscience*, *13*, 1179069519859371. https://doi.org/10.1177/1179069519859371

Heinilä, E., & Parviainen, T. (2022). *Meggie – easy-to-use graphical user interface for M/EEG analysis based on MNE-python* (p. 2022.09.12.507592). bioRxiv. https://doi.org/10.1101/2022.09.12.507592

Hill, A. T., Clark, G. M., Bigelow, F. J., Lum, J. A. G., & Enticott, P. G. (2022). Periodic and aperiodic neural activity displays age-dependent changes across early-to-middle childhood. *Developmental Cognitive Neuroscience*, *54*, 101076. https://doi.org/10.1016/j.dcn.2022.101076

Jenkinson, N., Kühn, A. A., & Brown, P. (2013). Gamma oscillations in the human basal ganglia. *Experimental Neurology*, *245*, 72–76. https://doi.org/10.1016/j.expneurol.2012.07.005

Jiang, B., Huang, Z. J., Morales, B., & Kirkwood, A. (2005). Maturation of GABAergic transmission and the timing of plasticity in visual cortex. *Brain Research Reviews*, *50*(1), 126–133. https://doi.org/10.1016/j.brainresrev.2005.05.007

Jones, E. G. (1993). GABAergic Neurons and Their Role in Cortical Plasticity in Primates. *Cerebral Cortex*, *3*(5), 361–372. https://doi.org/10.1093/cercor/3.5.361-a

Kahana, M. J. (2006). The Cognitive Correlates of Human Brain Oscillations. *Journal of Neuroscience*, *26*(6), 1669–1672. https://doi.org/10.1523/JNEUROSCI.3737-05c.2006

Katada, A., Ozaki, H., Suzuki, H., & Suhara, K. (1981). Developmental characteristics of normal and mentally retarded children's EEGs. *Electroencephalography and Clinical Neurophysiology*, *52*(2), 192–201. https://doi.org/10.1016/0013-4694(81)90166-8

Lamsa, K., Heeroma, J. H., & Kullmann, D. M. (2005). Hebbian LTP in feed-forward inhibitory interneurons and the temporal fidelity of input discrimination. *Nature Neuroscience*, *8*(7), 916–924. https://doi.org/10.1038/nn1486

Larsen, B., Cui, Z., Adebimpe, A., Pines, A., Alexander-Bloch, A., Bertolero, M., Calkins, M. E., Gur, R. E., Gur, R. C., Mahadevan, A. S., Moore, T. M., Roalf, D. R., Seidlitz, J., Sydnor, V. J., Wolf, D. H., & Satterthwaite, T. D. (2022). A developmental reduction of the excitation:inhibition ratio in association cortex during adolescence. *Science Advances*, *8*(5), eabj8750. https://doi.org/10.1126/sciadv.abj8750

Lendner, J. D., Helfrich, R. F., Mander, B. A., Romundstad, L., Lin, J. J., Walker, M. P., Larsson, P. G., & Knight, R. T. (2020). An electrophysiological marker of arousal level in humans. *eLife*, *9*, e55092. https://doi.org/10.7554/eLife.55092

Maes, C., Hermans, L., Pauwels, L., Chalavi, S., Leunissen, I., Levin, O., Cuypers, K., Peeters, R., Sunaert, S., Mantini, D., Puts, N. A. J., Edden, R. A. E., & Swinnen, S. P. (2018). Age-related differences in GABA levels are driven by bulk tissue changes. *Human Brain Mapping*, *39*(9), 3652–3662. https://doi.org/10.1002/hbm.24201

Mamiya, P. C., Richards, T. L., Edden, R. A. E., Lee, A. K. C., Stein, M. A., & Kuhl, P. K. (2021). *Task-related excitatory/inhibitory ratios in the fronto-striatal circuitry predict attention control deficits in attention-deficit/hyperactivity disorder* (p. 2021.03.25.21254355). medRxiv. https://doi.org/10.1101/2021.03.25.21254355

Manning, J. R., Jacobs, J., Fried, I., & Kahana, M. J. (2009). Broadband Shifts in Local Field Potential Power Spectra Are Correlated with Single-Neuron Spiking in Humans. *Journal of Neuroscience*, *29*(43), 13613–13620. https://doi.org/10.1523/JNEUROSCI.2041-09.2009

Manyukhina, V. O., Prokofyev, A. O., Galuta, I. A., Goiaeva, D. E., Obukhova, T. S., Schneiderman, J. F., Altukhov, D. I., Stroganova, T. A., & Orekhova, E. V. (2022). Globally elevated excitation–inhibition ratio in children with autism spectrum disorder and below-average intelligence. *Molecular Autism*, *13*(1), 20. https://doi.org/10.1186/s13229-022-00498-2

Marty, A., & Llano, I. (2005). Excitatory effects of GABA in established brain networks. *Trends in Neurosciences*, *28*(6), 284–289. https://doi.org/10.1016/j.tins.2005.04.003

Mayford, M., Siegelbaum, S. A., & Kandel, E. R. (2012). Synapses and Memory Storage. *Cold Spring Harbor Perspectives in Biology*, *4*(6), a005751. https://doi.org/10.1101/cshperspect.a005751

McGinley, M., Hoffman, R. L., Russ, D. W., Thomas, J. S., & Clark, B. C. (2010). Older adults exhibit more intracortical inhibition and less intracortical facilitation than young adults. *Experimental Gerontology*, *45*(9), 671–678. https://doi.org/10.1016/j.exger.2010.04.005

McSweeney, M., Morales, S., Valadez, E. A., Buzzell, G. A., & Fox, N. A. (2021). Longitudinal age- and sex-related change in background aperiodic activity during early adolescence. *Developmental Cognitive Neuroscience*, *52*, 101035. https://doi.org/10.1016/j.dcn.2021.101035

Merkin, A., Sghirripa, S., Graetz, L., Smith, A. E., Hordacre, B., Harris, R., Pitcher, J., Semmler, J., Rogasch, N. C., & Goldsworthy, M. (2021). *Age differences in aperiodic neural activity measured with resting EEG* (p. 2021.08.31.458328). bioRxiv. https://doi.org/10.1101/2021.08.31.458328

Merkin, A., Sghirripa, S., Graetz, L., Smith, A. E., Hordacre, B., Harris, R., Pitcher, J., Semmler, J.,

Rogasch, N. C., & Goldsworthy, M. (2022). Do age-related differences in aperiodic neural activity explain differences in resting EEG alpha? *Neurobiology of Aging*. https://doi.org/10.1016/j.neurobiolaging.2022.09.003

Merkin, A., Sghirripa, S., Graetz, L., Smith, A. E., Hordacre, B., Harris, R., Pitcher, J., Semmler, J., Rogasch, N. C., & Goldsworthy, M. (2023). Do age-related differences in aperiodic neural activity explain differences in resting EEG alpha? *Neurobiology of Aging*, *121*, 78–87. https://doi.org/10.1016/j.neurobiolaging.2022.09.003

Muthukumaraswamy, S. (2013). High-frequency brain activity and muscle artifacts in MEG/EEG: A review and recommendations. *Frontiers in Human Neuroscience*, *7*. https://doi.org/10.3389/fnhum.2013.00138

Ott, L. R., Penhale, S. H., Taylor, B. K., Lew, B. J., Wang, Y.-P., Calhoun, V. D., Stephen, J. M., & Wilson, T. W. (2021). Spontaneous cortical MEG activity undergoes unique age- and sex-related changes during the transition to adolescence. *NeuroImage*, *244*, 118552. https://doi.org/10.1016/j.neuroimage.2021.118552

Parviainen, T., Helenius, P., & Salmelin, R. (2019). Children show hemispheric differences in the basic auditory response properties. *Human Brain Mapping*, *40*(9), 2699–2710. https://doi.org/10.1002/hbm.24553

Pathania, A., Euler, M. J., Clark, M., Cowan, R. L., Duff, K., & Lohse, K. R. (2022). Resting EEG spectral slopes are associated with age-related differences in information processing speed. *Biological Psychology*, *168*, 108261. https://doi.org/10.1016/j.biopsycho.2022.108261

Rubenstein, J. L. R., & Merzenich, M. M. (2003). Model of autism: Increased ratio of excitation/inhibition in key neural systems. *Genes, Brain and Behavior*, *2*(5), 255–267. https://doi.org/10.1034/j.1601-183X.2003.00037.x

Schaworonkow, N., & Voytek, B. (2021). Longitudinal changes in aperiodic and periodic activity in electrophysiological recordings in the first seven months of life. *Developmental Cognitive Neuroscience*, *47*, 100895. https://doi.org/10.1016/j.dcn.2020.100895

Sohal, V. S., & Rubenstein, J. L. R. (2019). Excitation-inhibition balance as a framework for investigating mechanisms in neuropsychiatric disorders. *Molecular Psychiatry*, *24*(9), Article 9. https://doi.org/10.1038/s41380-019-0426-0

Spriggs, M. J., Cadwallader, C. J., Hamm, J. P., Tippett, L. J., & Kirk, I. J. (2017). Age-related alterations in human neocortical plasticity. *Brain Research Bulletin*, *130*, 53–59. https://doi.org/10.1016/j.brainresbull.2016.12.015

Tada, M., Kirihara, K., Koshiyama, D., Fujioka, M., Usui, K., Uka, T., Komatsu, M., Kunii, N., Araki, T., & Kasai, K. (2020). Gamma-Band Auditory Steady-State Response as a Neurophysiological Marker for Excitation and Inhibition Balance: A Review for Understanding Schizophrenia and Other Neuropsychiatric Disorders. *Clinical EEG and Neuroscience*, *51*(4), 234–243. https://doi.org/10.1177/1550059419868872

Taki, Y., & Kawashima, R. (2012). Brain Development in Childhood. *The Open Neuroimaging Journal*, *6*, 103. https://doi.org/10.2174/1874440001206010103

Tatti, R., Haley, M. S., Swanson, O. K., Tselha, T., & Maffei, A. (2017). Neurophysiology and Regulation of the Balance Between Excitation and Inhibition in Neocortical Circuits. *Biological Psychiatry*, *81*(10), 821–831. https://doi.org/10.1016/j.biopsych.2016.09.017

van Bijnen, S., Parkkonen, L., & Parviainen, T. (2022). Activity level in left auditory cortex predicts behavioral performance in inhibition tasks in children. *NeuroImage*, *258*, 119371. https://doi.org/10.1016/j.neuroimage.2022.119371

Voytek, B., Kramer, M. A., Case, J., Lepage, K. Q., Tempesta, Z. R., Knight, R. T., & Gazzaley, A. (2015). Age-Related Changes in 1/f Neural Electrophysiological Noise. *Journal of Neuroscience*, *35*(38), 13257–13265. https://doi.org/10.1523/JNEUROSCI.2332-14.2015

Walther, M., Berweck, S., Schessl, J., Linder-Lucht, M., Fietzek, U. M., Glocker, F. X., Heinen, F., & Mall, V. (2009). Maturation of inhibitory and excitatory motor cortex pathways in children. *Brain and Development*, *31*(7), 562–567. https://doi.org/10.1016/j.braindev.2009.02.007

Waschke, L., Donoghue, T., Smith, S., Voytek, B., & Obleser, J. (2019). Aperiodic EEG activity tracks 1/f stimulus characteristics and the allocation of cognitive resources. *2019 Conference on Cognitive Computational Neuroscience*. 2019 Conference on Cognitive Computational Neuroscience, Berlin, Germany. https://doi.org/10.32470/CCN.2019.1111-0

Wilkinson, C. L., & Nelson, C. A. (2021). Increased aperiodic gamma power in young boys with Fragile X Syndrome is associated with better language ability. *Molecular Autism*, *12*(1), 17. https://doi.org/10.1186/s13229-021-00425-x

Xing, W., de Lima, A. D., & Voigt, T. (2021). The Structural E/I Balance Constrains the Early Development of Cortical Network Activity. *Frontiers in Cellular Neuroscience*, *15*, 687306. https://doi.org/10.3389/fncel.2021.687306

APPENDICES

Appendix 1. *Descriptive statistics of the variable offset*

		M	SD	MD	MIN	MAX
Younger children	left frontal	-23.37	0.0553	-23.448	-23.957	-22.761
	right frontal	-23.43	0.0546	-23.445	-24.086	-22.722
	left occipital	-22.97	0.0751	-22.858	-23.816	-22.157
	right occipital	-22.00	0.0793	-22.892	-23.849	-22.262
Older children	left frontal	-23.570	0.2586	-23.592	-24.100	-22.964
	right frontal	-23.582	0.2635	-23.629	-24.100	-23.015
	left occipital	-23.067	0.4015	-23.061	-24.028	-22.306
	right occipital	-23.098	0.4451	-23.103	-24.289	-22.257
Adults	left frontal	-23.876	0.1588	-23.911	-24.154	-23.617
	right frontal	-23.908	0.1936	-23.967	-24.189	-23.582
	left occipital	-23.387	0.2506	-23.435	-23.667	-22.726
	right occipital	-23.418	0.2459	-23.447	-23.766	-22.712

Appendix 2.. *Descriptive statistics of the variable exponent*

		M	SD	MD	MIN	MAX
Younger children	left frontal	1.191	0.1320	1.153	0.962	1.480
	right frontal	1.192	0.1336	1.187	0.968	1.439
	left occipital	1.358	0.2520	1.354	0.644	1.846
	right occipital	1.355	0.2428	1.380	0.716	1.796
Older children	left frontal	1.112	0.1075	1.092	0.898	1.343
	right frontal	1.109	0.1106	1.100	0.859	1.349
	left occipital	1.309	0.1707	1.296	1.021	1.691
	right occipital	1.277	0.1856	1.256	0.950	1.677
Adults	left frontal	0.913	0.0794	0.9120	0.810	1.073
	right frontal	0.902	0.0810	0.8890	0.810	1.058
	left occipital	1.040	0.1809	1.034	0.787	1.484
	right occipital	1.017	0.1653	1.002	0.788	1.460