



Research Paper



Two are better than one: Differences in cortical EEG patterns during auditory and visual verbal working memory processing between Unilateral and Bilateral Cochlear Implanted children

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ABSTRACT

Despite the proven effectiveness of cochlear implant (CI) in the hearing restoration of deaf or hard-of-hearing (DHH) children, to date, extreme variability in verbal working memory (VWM) abilities is observed in both unilateral and bilateral CI user children (CIs). Although clinical experience has long observed deficits in this fundamental executive function in CIs, the cause to date is still unknown. Here, we have set out to investigate differences in brain functioning regarding the impact of monaural and binaural listening in CIs compared with normal hearing (NH) peers during a three-level difficulty n-back task undertaken in two sensory modalities (auditory and visual). The objective of this pioneering study was to identify electroencephalographic (EEG) marker pattern differences in visual and auditory VWM performances in CIs compared to NH peers and possible differences between unilateral cochlear implant (UCI) and bilateral cochlear implant (BCI) users. The main results revealed differences in theta and gamma EEG bands. Compared with hearing controls and BCIs, UCIs showed hypoactivation of theta in the frontal area during the most complex condition of the auditory task and a correlation of the same activation with VWM performance. Hypoactivation in theta was also observed, again for UCIs, in the left hemisphere when compared to BCIs and in the gamma band in UCIs compared to both BCIs and NHs. For the latter two, a correlation was found between left hemispheric gamma oscillation and performance in the audio task. These findings, discussed in the light of recent research, suggest that unilateral CI is deficient in supporting auditory VWM in DHH. At the same time, bilateral CI would allow the DHH child to approach the VWM benchmark for NH children. The present study suggests the possible effectiveness of EEG in supporting, through a targeted approach, the diagnosis and rehabilitation of VWM in DHH children.

1. Introduction

Sensory perception results from the interaction between sensory input and ongoing brain cortical activity (Yusuf et al., 2017), and it is widely understood that the lack of input from one sensory modality profoundly impacts brain development (Bavelier and Neville, 2002; Bonna et al., 2021). In the case of congenital deafness, there is evidence from animal and human studies that early auditory deprivation leads to an atypical organisation of the auditory nervous system (Kral and Sharma, 2012; Gilley and Sharma, 2008). Indeed, congenital deafness

deprives the child of acoustic input during a sensitive developmental period that requires auditory experience to acquire fundamental skills such as language (Kral, 2013). However, the effects of impaired hearing go far beyond just difficulty in speech recognition (Wingfield and Peelle, 2015). In fact, auditory deprivation impacts numerous pathways such as brain structure, neural processing, and behaviour (Köse et al., 2022), affecting neurocognitive development in children across several related domains, including auditory, linguistic, cognitive, social, literacy, and academic functioning (Fitzpatrick, 2015). The Cochlear Implant (CI), a prosthetic device that electrically stimulates the auditory nerve via a set

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of electrodes placed in the cochlea (Zeng, 2011), is universally considered to be the standard of care for the medical treatment of severe-to-profound sensory-neural hearing loss in children and adults (Pisoni et al., 2018).

Although CI allows stimulation of the auditory nerve and thus the development of the brain cortices in children who are deaf or hard of hearing (DHH) (Wilson and Dorman, 2008), enabling communication skills (Geers and Nicholas, 2013; Kronenberger et al., 2018; Sharma et al., 2020), there are notable variations in language and neurocognitive outcomes (Tamati et al., 2022; Szagun and Schramm, 2016; McCreery and Walker, 2022). The factors contributing to this are not yet fully understood (Clearly et al., 2000; McCreery and Walker, 2022). In fact, although the differences present in many clinical outcomes can be attributed to several factors such as age at implantation (Kral, 2007), length of device use (Calmels et al., 2004), binaural or monoaural CI (Litovsky and Gordon, 2016), type of bilateral CI surgery (e.g. simultaneous or sequential, Killan et al., 2019), the onset of hearing loss (Dowell et al., 2002), residual hearing (Zwolan et al., 1997), speech processing strategy (Hu et al., 2011) and non-verbal intelligence (Castellanos et al., 2016), considerable unexplained variability remains today (Faulkner and Pisoni, 2013).

Consequently, in recent years, neurocognitive factors contributing to language outcomes have been of considerable interest to researchers and clinicians because they offer a potential target for intervention that can help explain and improve language outcomes in DHH children (Jamsek et al., 2022).

One domain of neurocognitive functioning that supports language development in DHH populations concerns a broad set of neurocognitive abilities (executive functions) including working memory, inhibition, and shifting (Suchy et al., 2009; Miyake et al., 2000; Solís-Campos et al., 2023).

Working memory (WM) is a system within the brain necessary for holding and manipulating information while performing various tasks (Baddeley and Hitch, 1974; Baddeley and Della Sala, 1996; Baddeley, 2010). It is fundamental to higher cognitive functions, including reasoning and reading comprehension (Engle et al., 1999; 2002; Just and Carpenter, 1992; Kyllonen and Christal, 1990), and is linked to the development of academic abilities (Hitch et al., 2001; Thomason et al., 2009).

Regarding the interaction of sensory and cognitive systems, the amount and nature of auditory input after receiving a CI affects the encoding and processing of verbal material in WM, especially for children (Burkholder and Pisoni, 2003; Pisoni and Cleary, 2004). Specifically, verbal working memory (VWM)—commonly defined (Schwering and MacDonald, 2020) as the temporary maintenance of verbal information (i.e. some aspects of language)—is comprised of two components: phonological storage which allows for the brief repository of speech content and an articulatory rehearsal mechanism allowing for silent rehearsal to occur in order for stored information to be maintained. Research has shown that VWM has a vital function during the language acquisition process facilitating the extended learning of new vocabulary (Baddeley et al., 1998). As Akçakaya et al. (2019, p.2) noted, when a perceptual limitation such as hearing loss occurs, difficulties in coding may affect the language functions of storage, recall and processing, thereby affecting the relationship between VWM and vocabulary knowledge. Moreover, VWM for both auditory signals and visual text is expected to engage the phonological loop, in which verbal information can be stored using active rehearsal or subvocalization of inner speech. (Baddeley, 2000; Baddeley et al., 1974).

An extensive body of research has demonstrated that groups of children with CI show VWM delays relative to matched groups of normal hearing (NH) peers (Herran et al., 2023). Furthermore, significant variability and individual differences in VWM skills are found within the population of CI users (Pisoni et al., 2018; Kronenberger and Pisoni, 2018). Specifically, some results of studies show that in children with CI, a moderate correlation between VWM and speech perception,

production and comprehension (Pisoni and Geers, 2000) and a strong positive correlation between speech perception and VWM (Pisoni and Cleary, 2003) even when statistical analysis is controlled for demographic and audiological variables. Consequently, VWM has been identified as a key neurocognitive risk domain and a potential target for intervention to improve spoken language outcomes in CI users (Romano et al., 2021). It is becoming evident in the international field of CI research that individual differences and variations in speech and language outcomes following CI are not merely an “ear issue” that deals with sensory coding and processing operations, reflecting the upstream contributions from the peripheral auditory pathways (Pisoni et al., 2017): the sources of that variability will not be understood until the interactions between spoken language and cognitive functions can be taken into account (Nittrouer et al., 2017). However, despite such robust evidence regarding the involvement of deficit and increased variability in VWM performance in children with CI, the underlying neural processes still remain obscure. In fact, previously cited studies have addressed WM deficits in children with CI by psychometric (e.g. digit span) and speech test assessments (Pisoni and Cleary 2003; Di Stadio et al., 2020; Herran et al., 2023). Furthermore, despite the validated perceptual benefits provided by cochlear implantation to the perceptual and cognitive development of children with deafness, to our knowledge, no study has compared the performance of children with one and two cochlear implants in VWM tasks. In our opinion, such comparison is a crucial point for understanding cortical plasticity in subjects with sensory deficits such as hearing loss or deafness.

Indeed, binaural hearing gives three major cues: head shadow effect (HSE), binaural squelch effect (BSQ) and binaural summation effect (BSU), which enhance hearing performance in patients with normal hearing (Brown and Balkany, 2007), providing better sound source localization and better speech-in noise understanding (Ching et al., 2007). Considering this evidence, it is intuitive how brain activity can be significantly different between UCI and BCI users, raising the question of whether the contribution of two implants develops VWM neurophysiological patterns comparable to those of a typically developing brain.

Thanks to the recent use of electroencephalography (EEG), a powerful, accessible and versatile neuroimaging tool for exploring human brain physiology, cognition and behaviour (Biasucci et al., 2019), it has been possible to neurophysiologically investigate perceptual and cognitive deficits in children with CI obtaining quantitative data on brain activity during VWM tasks while avoiding the bias inherent in face-to-face psychometric tests administration. Specifically, EEG provides an especially rich set of features for allowing the assessment of cognitive processes (Šneidere et al., 2020) and for indexing the complex set of brain correlates that underline listening (Wisniewski et al., 2018).

EEG measures the electric potential on the surface of the scalp generated (in part) by neural activity originating from the brain during communications between neurons. EEG power is typically split into bands defined as the delta (δ : 1–4 Hz), theta (θ : 4–8 Hz), alpha (α : 8–13 Hz), beta (β : 13–20 Hz), and gamma (γ : >20 Hz) which correspond to different spectral peaks that relate to behaviour or cognitive state (Nunez et al., 2016) depending on the brain regions considered (see Poldrack, 2010 about understanding the functional anatomy of mental functions). For example, alpha oscillations have been shown to play a key role in inhibiting nonessential processing, which in turn facilitates task performance (Klimesch et al., 2007). This rhythm is related to the gating of perceptual awareness and attentional control (Grimshaw et al., 2014) and so could be considered an index of top-down processing (Bazanov and Vernon, 2014). Delta oscillations are prominent in early developmental stages and in slow-wave sleep and are implicated in salience detection and subliminal perception (Knyazev, 2012).

Theta rhythm has shown its relevance in spatial navigation (Do et al., 2021) ostensibly in memory processes (Klimesch et al., 1994, 1997; Osipova et al., 2006; Jensen and Tesche, 2002; Sederberg et al., 2003)

and attention (Pennekamp et al., 1994; Gevins et al., 1997; Sauseng et al., 2007). Specifically, memory-related theta activity is most consistently reported in episodic long-term memory and working memory (Sauseng et al., 2010), for a review on functional correlates of theta waves see (Karakaş, 2020).

Regarding the beta-band, many classical observations have linked this rhythm to motor functions (Engel and Fries, 2010; Barone and Rossiter, 2021). Finally, gamma band has been found to reveal correlates of processes associated with binding phenomena (Herrmann, 2003). Because the power in the gamma band increases during complex and attention-demanding tasks, induced gamma activity is often interpreted as the neural substrate of cognitive processes (Tallon-Baudry and Bertrand (1999) playing an important role in attention and both working and long-term memory (Jensen et al., 2007). Specifically, some of the abilities relevant to working memory performance have been associated with oscillatory neural activity, especially in the gamma band (Thomson et al., 2021). Moreover, it has been demonstrated that gamma reflects local excitatory–inhibitory cortical interactions which may support communications between cortical areas and in turn support a number of cognitive processes (Thomson et al., 2021), and greater gamma-band activity means greater facilitation for attended auditory stimuli (Golombic et al., 2013). Furthermore, the left hemisphere compared to the right exhibits a more widely distributed and more engaged language network: in most people, the left cerebral hemisphere plays a dominant role in speech (Qi and Legault, 2020) and hemispheric specialization has been investigated through EEG (Donchin et al., 1977; Morillon et al., 2010).

In line with the non-exhaustive features described so far, EEG in recent times has also been considered a useful tool for interdisciplinary investigation into the cortical dynamics underlying cognitive and perceptual processes in CI patients. Alpha activity for example would predict both the ability to perceive speech in noise and listening effort (LE) — defined as the deliberate allocation of mental resources to overcome obstacles in goal pursuit when carrying out a listening task (Pichora-Fuller, 2006; Dimitrijevic et al., 2019; Wisniewski and Zakrzewski, 2023), while Wisniewski et al., 2015 identified frontal midline theta power as an LE index. Moreover, theta and alpha connectivity were used to differentiate performances between different CI processors (Maglione et al., 2017), while Wöstmann et al. (2015) observed that alpha power varied proportionately with self-reported LE in a listening task that altered speech spectral detail. Furthermore, during a word-identification task, a lower level of activity in parietal alpha was observed in the most challenging listening condition (Marsella et al., 2017) while neural entrainment to speech envelope has been associated with successful selective attention in dichotic listening tasks (Petersen et al., 2017). Furthermore, Cartocci et al. (2019) showed a correlation between the period of deafness and the asymmetry of cortical activity towards the side of the hearing ear in the frontal, parietal and occipital areas. Moreover, an EEG workload index (theta/alpha ratio) showed higher values in situations of excessive noisy environment during a word recognition task (Cartocci et al., 2015). It has also been applied in studies on music perception in CI users (Inguscio et al., 2022b). Furthermore, in the field of affective auditory neuroscience, hemispheric gamma activation has been shown to suggest a sensitive period for CI intervention for the better development of emotion recognition skills (Cartocci et al., 2021).

Focusing more on EEG and WM, it has been proposed that brain oscillations likely play a significant role in the storage of information in WM (Li and Curtis, 2023; Pavlov and Kotchoubey, 2022). Experimentally, oscillations in various frequency bands (alpha, theta, gamma) have been shown to be modulated differently during WM tasks, but their exact functional role remains to be determined (Jokisch and Jemsen, 2007; Jensen, 2006; Roux and Uhlhaas, 2014). Furthermore, VWM research strongly supports the hypothesis as to the involvement of theta oscillations in WM maintenance processes (Pavlov and Kotchoubey, 2022) although some studies have found no observable and/or

statistically significant gradual increases (Kwon et al., 2015; Schack and Klimesch, 2002). Moreover, EEG oscillations in the theta frequency range are related to WM tasks (Sauseng et al., 2004); for a review of evidence, see (Klimesch, 1999). Specifically, theta power enhancement is related to memory performance (Itthipuripat et al., 2013), as well as to task difficulty (Gevins et al., 1997; Jensen and Tesche, 2002) and WM maintenance processes (see the recent systematic review by Pavlov and Kotchoubey et al., 2022). Notably, as is well documented in the literature, in the frontal scalp theta band power increases with memory load and mental effort (Raghavachari et al., 2001; Jensen and Tesche, 2002; Onton et al., 2005; Zakrzewska and Brzezicka, 2014; Smith and Jonides, 1999; Berger and Sauseng, 2022). Moreover, attentional processes engage frontal areas involved in the generation of theta oscillations (Klimesch, 1999; Gevins et al., 1997; Smith and Jonides, 1999) and the frontal theta amplitude is linearly correlated with WM load (Xie et al., 2021): therefore frontal theta band power is a promising neural measure to assess attentional processing (Meyer et al., 2023).

WM retention also has an effect on alpha power, although the direction of this effect is inconsistent across studies (Pavlov and Kotchoubey, 2022). Most studies indeed report gradual changes in alpha power in line with theta but evidence suggest that alpha modulation depends on the type of stimulus presentation (Okuhata et al. 2013). Moreover given the association between the alpha rhythm and cortical inhibition, these findings are consistent with greater activation of task-relevant cortical areas with higher WM demands (Kosachenko et al., 2023). Finally, in children (< 14 years old), alpha oscillations have been linked to patterns of lateralization in the maintenance of working memory (Sander et al., 2012).

Beta oscillations in VWM research are much less studied than alpha and theta oscillations and show a wide diversity of effects (Pavlov and Kotchoubey, 2022) in addition to being associated more with spatial WM (Proskovec et al., 2018). Activity in the gamma band has been hypothesized to directly reflect the neuronal correlate of maintained working memory representations (Jokisch and Jensen, 2007) and appears to have a universal role for sensory and cognitive processing (Karakaş and Başar, 1998; Başar et al., 2000; Miller et al., 2018). Moreover, some of the abilities relevant for working memory performance have been associated with oscillatory neural activity, especially in the gamma band (Thomson et al., 2021). Specifically, it has been demonstrated that gamma reflects local excitatory–inhibitory cortical interactions which may support communications between cortical areas and in turn support a number of cognitive processes (Thomson et al., 2021) and greater gamma-band activity means greater facilitation for attended auditory stimuli (Golombic et al., 2013).

Focusing briefly on the brain areas most related to WM processing, a widely held view of prefrontal cortex (PFC) function is that it encodes task relevant information in working memory (Goldman-Rakic, 1987). Specifically, the dorsolateral PFC, due to its connection with the parietal cortex plays a crucial role in both verbal and visuospatial WM (Barbey et al., 2013; Sauseng et al., 2005) see Lara & Wallis (2015) for a review on the role of PFC in WM. Furthermore, it would appear that powerful frontoparietal synaptic connectivity may be one of the mechanisms involved in the development of WM ability during infancy (Edin et al., 2009). In addition, mapping PFC and sensory cortices, some areas showed specificity for the modality of sensory stimuli (Linden, 2007; Klingberg, 2010), while studies have shown involvement of occipital cortices in task-modulated mnemonic representations (Yu and Shim, 2017).

Furthermore, it has been observed that children and adults exhibited similar hemispheric asymmetry during WM activation, greater on the right for spatial WM and on the left for VWM (Thomason et al., 2009; Nagel et al., 2013). Finally, the left hemisphere compared to the right exhibits a more widely distributed and more engaged language network in most people; it playing a dominant role in speech (Qi and Legault 2020) and hemispheric specialization having been frequently investigated through EEG (Donchin et al., 1977; Morillon et al., 2010).

While investigation of the neural correlates of WM in children is rare, particularly in clinical groups of children (Inguscio et al., 2021), no study to our knowledge specifically investigates bimodal VWM performance simultaneously in children with one and two cochlear implants.

For example, in one previous study conducted by our group an electrophysiological benchmark of the VWM in typical NH children was sought for auditory and visual stimuli, while in another, we compared the neurophysiological correlates of VWM between NH and UCI (Inguscio et al., 2021, 2022a).

To date, as far as we are aware, no study has investigated the neurophysiological correlates of auditory and visual VWM, comparing children with unilateral and bilateral cochlear implantation. Considering the crucial role of VWM in the development of essential skills such

as language, and the importance of sensory stimulation for the proper structuring of high-level cognitive processes and the cross-modal plasticity that DHH children go through, in this study, we investigated for the first time the cortical activation pattern of VWM on unilateral and bilateral CI children with the primary pioneering aim of exploring as to whether and how the EEG and behavioural correlates of visual and auditory verbal stimuli in children with CI:

- i. differ or not from children with normal hearing depending on the sensory modality of the stimulation;
- ii. differ between unilateral and bilateral implant recipients.

The secondary aim was to test whether any differences found in the

Table 1

Demographic and clinical data concerning 16 patients (P) and demographic data concerning the 11 normal hearing children (NH) assigned to the control group. In particular the table indicates gender (*M*=male; *F*=female), chronological (CHRON.) age, unilateral or bilateral cochlear implant (CI) use, receiver (REC.) and processor (PROC.) model (MOD) of CI, onset, degree and aetiology of deafness (O.D.), age at CI, auditory (AUD.) age (years of CI use since implantation), schooling level (SCH.) and year attended.

	Gender	CHRON. AGE	CI	CI REC. MOD.	CI PROC. MOD.	Onset O.D.	DEGREE O.D.	Aetiology O.D.	Age at CI	AUD. AGE	SCH.
P1	F	12.00	Unilateral	AB HiRes 90K	Naida CIQ 90	Congenital	Profound	Homozygous Cx26 gene mutation	2.90	9.09	Secondary (first year)
P2	F	10.73	Unilateral	AB HiRes 90K	Naida CIQ 90	Congenital	Profound	Homozygous Cx26 gene mutation	1.86	8.87	Primary (fifth year)
P3	F	11.49	Unilateral	CI24RE	Nucleus CP 1000	Congenital	Profound	Homozygous Cx26 gene mutation	1.41	10.07	Secondary (first year)
P4	F	11.14	Unilateral	CI24RE	Nucleus CP 1000	Congenital	Profound	Homozygous Cx26 gene mutation	1.41	10.07	Secondary (first year)
P5	F	11.58	Unilateral	AB HiRes 90K	Naida CIQ 90	Congenital	Profound	Homozygous Cx26 gene mutation	1.16	9.97	Secondary (first year)
P6	M	10.09	Unilateral	AB HiRes 90K	Naida CIQ 90	Congenital	Profound	Usher syndrome	0.79	10.78	Primary (fourth year)
P7	F	8.97	Unilateral	CI24RE	Nucleus CP 1000	Congenital	Profound	Unknown	1.79	8.30	Primary (third year)
P8	M	8.97	Bilateral	CI24RE	Nucleus CP 1000	Congenital	Profound	Homozygous Cx26 gene mutation	1.6	7.66	Primary (third year)
P9	M	10.79	Bilateral	AB HiRes 90K	Naida CIQ 90	Congenital	Profound	Unknown	4.17	6.63	Primary (fifth year)
P10	M	13.89	Bilateral	AB HiRes 90K	Naida CIQ 90	Congenital	Profound	Unknown	3.25	10.68	Secondary (first year)
P11	M	7.35	Bilateral	AB HiRes 90K	Naida CIQ 90	Congenital	Profound	Homozygous Cx26 gene mutation	1.41	5.79	Primary (second year)
P12	F	9.93	Bilateral	sincrony sonnet	Sonnet 2	Congenital	Profound	Homozygous Cx26 gene mutation	1.58	10.52	Primary (fourth year)
P13	M	11.95	Bilateral	AB HiRes 90K	Naida CIQ 90	Congenital	Profound	Homozygous Cx26 gene mutation	2.08	9.84	Secondary (first year)
P14	F	8.56	Bilateral	AB HiRes 90K	Naida CIQ 90	Congenital	Profound	Cytomegalovirus infection	2.17	6.7	Primary (third year)
P15	M	7.59	Bilateral	Mi10 Flex28	Sonnet 2	Congenital	Profound	Homozygous Cx26 gene mutation	2.17	6.39	Primary (second year)
P16	F	8.07	Bilateral	Mi10 Flex28	Rondo 2	Congenital	Profound	Homozygous Cx26 gene mutation	2.58	6.56	Primary (second year)
NH1	F	10.1	–	–	–	–	–	–	–	–	Primary (fourth year)
NH2	M	12.64	–	–	–	–	–	–	–	–	Secondary (second year)
NH3	M	10,91	–	–	–	–	–	–	–	–	Primary (fifth year)
NH4	M	9.20	–	–	–	–	–	–	–	–	Primary (fourth year)
NH5	F	12.75	–	–	–	–	–	–	–	–	Secondary (second year)
NH6	M	10.99	–	–	–	–	–	–	–	–	Primary (fifth year)
NH7	F	7.97	–	–	–	–	–	–	–	–	Primary (second year)
NH8	F	11.51	–	–	–	–	–	–	–	–	Secondary (first year)
NH9	M	13.93	–	–	–	–	–	–	–	–	Secondary (third year)
NH10	M	8.26	–	–	–	–	–	–	–	–	Primary (second year)
NH11	F	10.84	–	–	–	–	–	–	–	–	Primary (fifth year)

investigation into the primary aim were related to deficiencies in lexical comprehension.

Investigating, through EEG, the relationship between the nervous system and mental processes and discovering whether there are any different patterns between UCI and BCI, could provide quantitative data on the effectiveness of bilateral vs unilateral CI in allowing for a more typical development of brain functions that are crucial for language and academic skills. In addition, it could provide evidence for concrete neurophysiological support for rehabilitation in CI users, ultimately contributing to auditory neuroscience research.

2. Materials and methods

2.1. Participants

A total of 30 children were recruited into the present study, all native Italian speakers and right-handed, who were divided into three groups: unilateral CI users (UCI), bilateral CI users (BCI), and hearing control (NH). The age of the participants was determined according to previous studies (Pelegrina et al., 2015; Yapple and Arsalidou, 2018; Inguscio et al., 2021). Three participants were subsequently excluded because of their lack of cooperation in the task training accomplishment. Therefore, the final experimental population was composed of 2 clinical samples: 7 UCI with CI on their right side (mean age 11.222 ± 0.634 years); 9 BCI (mean age 9.678 ± 2.189 years) and a control group of 11 NH (mean age 10.831 ± 1.872 years). Clinical data of patients are presented in Table 1.

Raven's standard progressive matrices (RPM) (Raven, 1998), a test of non-verbal spatial reasoning, was used at screening for participant selection. Finally, exclusion criteria for enrolment in the study were: diagnosis of neuropsychiatric disorders; scores below the standard average for their age (taken from the test norm) on RPM; left-handed children due to past evidence of handedness influence on cerebral laterality (Lux et al., 2008), the presence of visual sensory deficits in patients and finally presence of visual and/or auditory deficits in controls.

Participants and their parents were informed about the study before the experimental session. We obtained informed written consent from the parents and verbal assent from the children. Participation in the study was voluntary; children received a present after their involvement. The eligibility criteria for the clinical groups included congenital severe/profound deafness (Pure Tone Average in the better ear ≥ 80 dB HL for 500–4000 Hz), first CI by 3.5 years of age and second CI if bilaterally implanted, by six years of age. The age at CI criteria was chosen based on physiological studies suggesting that in the absence of typical auditory stimulation, there is a period of about 3.5 years during which the central auditory system retains its maximum plasticity and that this can extend up to 6–7 years after which it is significantly reduced (Sharma et al., 2002; 2005). Good speech perception abilities, defined as bisyllabic word recognition and sentence comprehension (Cutugno et al., 2000) $>90\%$ in a silent room at the moment of the EEG test; none of the UCI participants wore any hearing aid in the contralateral ear to the one with the CI. On the day of the EEG registration session, all the patients previously underwent variable-tone free-field and speech audiometry to ensure their hearing abilities were adequate. There were no significant differences between the clinical and control groups in terms of age [Kruskall Wallis H test: $H(2)=3.667$, $p = 0.160$] and between clinical groups for Age at CI [Mann Whitney U test: $U = 49.000$, $p = 0.071$] and for auditory age [Mann Whitney U test: $U = 15.000$, $p = 0.090$]. The EEG recordings were performed at Centro Impianti Cocleari of Policlinico Umberto I, Rome, according to the principles outlined in the Helsinki Declaration of 1975, revised in 2000, and approved by the Institutional Ethics Committee of Policlinico Umberto I- Rome (no. 259/2020).

2.2. Lexical comprehension

Lexical comprehension was assessed using the Italian version () of

the Peabody Picture Vocabulary Test (PPVT) (Dunn and Dunn, 1981). PPVT has been used in a variety of typically and atypically developing pediatric populations, and it has been used in numerous studies examining the vocabulary outcomes of children with hearing impairment (Cleary et al., 2000; Rudge et al., 2022). PPVT consisted of 175 black-and-white stimulus items, displaying four pictures per page with increasing difficulty. The examiner said a word, and then the examinee responded by pointing out the picture that she/he thought corresponded to the word presented by the examiner. PPVT is a test used in the assessment of language in Italian children with hearing impairment (Guerzoni et al., 2020; Nicastrì et al., 2023).

2.3. Verbal working memory task

During the EEG recording, participants performed two verbal n-back tasks (Kirchner, 1958), a popular measure of working memory (Yapple and Arsalidou, 2018) already used in children with CI (Inguscio et al., 2022a) with different memory loads from 0-back to 2-back: an auditory n-back task (AUD-task) in which stimuli were presented orally, and a visual n-back task (VID-task) in which stimuli were presented visually. The elegant properties of the n-back task have led to its extensive, wide-spread use as a tool to manipulate workload in neuroimaging (for a meta-analysis of brain regions involved in working memory, see Owen et al., 2005) and as a tool to measure cognitive performance under various conditions (e.g. Moore et al. 2009; Brouwer et al., 2012). The order of the task administration and the order of the n-back blocks presentation were randomised across participants.

Stimulus materials: verbal material consisted of auditory and visual stimuli, referring to seven consonants (c, g, k, p, q, t, v) already used in previous experimental protocols (Jaeggi et al., 2007, 2008, 2009, 2010). Vowels were excluded to reduce the likelihood of participants developing chunking strategies which reduce mental effort (Grimes et al., 2008). We conducted a stimuli exposure pretest before involvement in the study to ensure correct perception by clinical and control groups. Visual stimuli (Consolas font—130) with a duration of 500 ms and an interstimulus interval (ISI) of 3000 ms (Pelegrina et al., 2015) were presented one at a time on a grey background in the centre of a monitor screen placed at eye level, 50 cm from the participant. Auditory stimuli (duration 500 ms; ISI 2500) (Jaeggi et al., 2007) consisted of a recorded female voice, set at a 65 dB SPL intensity to ensure comfortable audibility to both NH and CI users (Cartocci et al., 2021), transmitted by two audio speakers placed at face level 1 m in front of the participant.

Task execution: For each stimulus, participants in the ISI had to respond by pressing a previously identified key (D/K) on the keyboard to indicate whether the letter was a target (K) or a nontarget (D); thus, there was a behavioural response in either case. In the 0-back condition, the letter X was the target. In the 1-back condition, a letter was a target when it was the same as the one presented immediately before. In the 2-back condition, a letter was a target when it was the same as the two letters before. With this version of the n-back task, the difficulty level varies without varying visual/auditory input or frequency and type of motor output (button presses). A 3-back condition was not used due to evidence that many adults find it too difficult and tend to give up (Ayaz et al., 2007; Izzetoglu et al., 2007). Participants received detailed instructions on how to perform the task correctly, and a training session was undertaken before the practical measurement session to familiarise themselves with the experimental procedure.

Task structure: Load levels (0, 1, 2-back) were presented in six blocks (2 for each level) for each task (auditory and visual). The blocks consisted of 21 randomised stimuli (30 % target) (Pelegrina et al., 2015). In the baseline phase, participants were asked to remain relaxed with no task to perform other than to look at the screen. At the same time, auditory or visual stimuli were presented, anticipating the task phase. During the baseline phase, the seven stimuli were repeated randomly three times (500 ms with 3000 ms ISI), creating a 21-item block analogous to the experimental blocks. The task phase then consisted of 2

randomised presentations of the three blocks. Thus, each session consisted of 3-n back levels per 2 presentations for six blocks in randomised order for audio and visual tasks. Half of the participants started with the visual stimuli task, and the other half with the auditory task (see Fig. 1 for task structure schematisation). A Lenovo PC (monitor resolution 1024 × 768) displayed and controlled stimuli presentation and collected participants' responses in terms of reaction times (RTs) and correct responses (CRs) through the software package E-Prime (Psychology Software Tools, Pittsburgh, PA, USA, Version 3.0).

Procedure: the participant was seated on a chair in an audiometric test room while the experimental design was fully explained. Participants were instructed to take a comfortable position and avoid unnecessary movement to reduce muscular artefacts in the EEG signal. After each task phase, the participant indicated the perceived task difficulty (easy–medium–hard) on a stylised image; at the end of the entire experimental session, they were asked to rate, through a stylised image of the level of difficulty, which of the two tasks (visual or auditory) was the most difficult.

2.4. Measures collections

2.4.1. Behavioural and language measures

We collected response latencies in terms of the following: Reaction Times (RTs, measured from the time of stimulus offset); performances in terms of accuracy (ACC) calculated as the percentage of correct responses for each task condition (each n-back level for auditory and visual modality tasks). A speech and language therapist administered PPVT.

2.4.2. EEG measures

EEG data was recorded from 20 electrodes (Fpz, Fz, F3, F4, F7, F8, Cz, C3, C4, T7, T8, Pz, P3, P4, P7, P8, Cp5, Cp6, O1 and O2) placed over the scalp at standard 10–20 locations (International Standard configuration, Jasper, 1958) referred to the participants' earlobes. The data were acquired at 256 Hz through each channel from a digital ambulatory monitoring system (BePlus System-EBNeuro, S.p.A., Firenze, Italy), the impedance was kept below 10kΩ and to remove power interference we applied a notch filter. The raw EEG signals were then filtered through a 5th order Butterworth band pass filter [1–45 Hz] to reject continuous

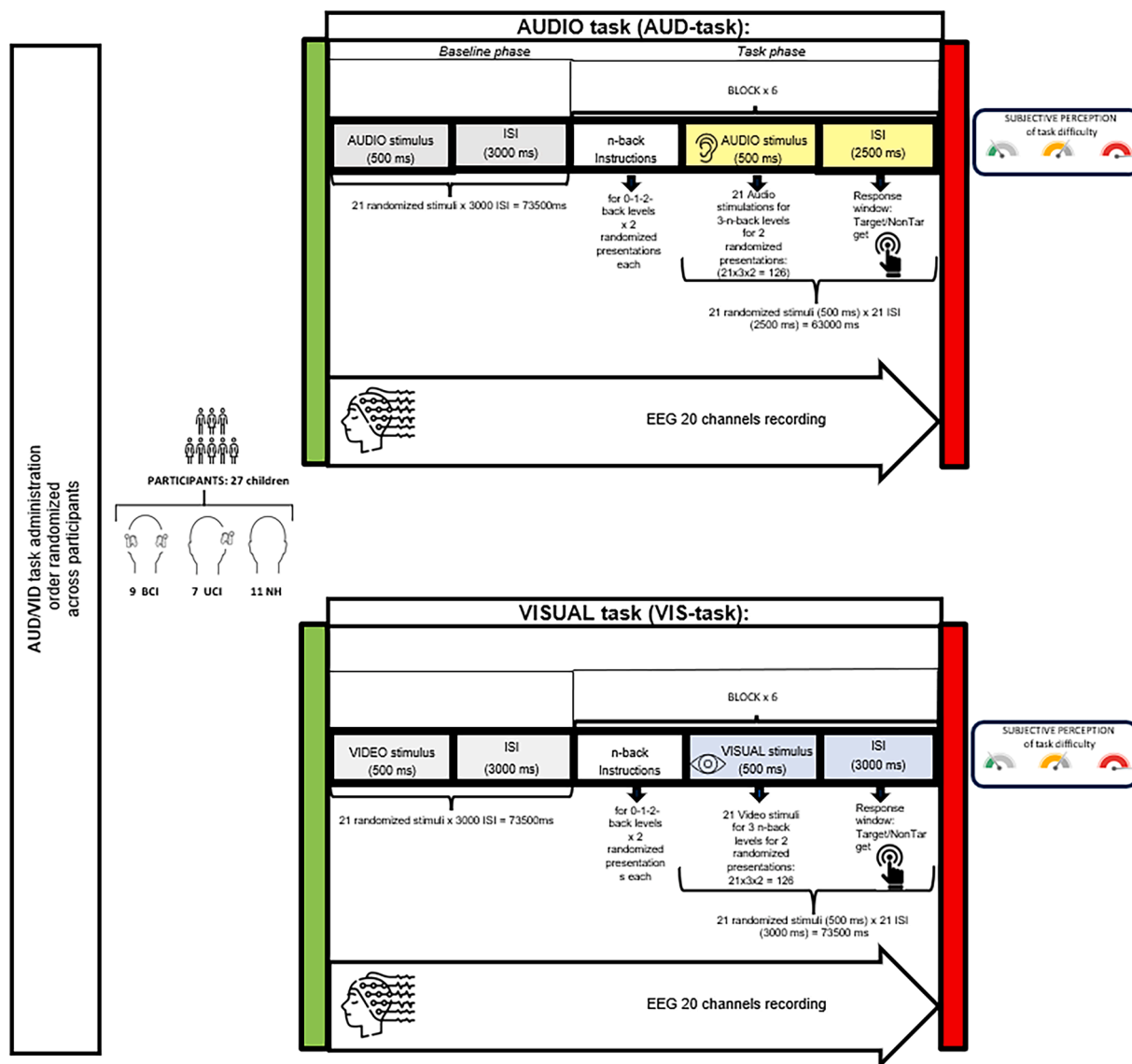


Fig. 1. Experimental design with the trial timeline. Schematic illustration for each n-back task (audio-AUD and video-VID) performed by participants divided into 3 groups (UCI=Unilateral cochlear implant; BCI=bilateral cochlear implant users; NH=normal hearing) during electroencephalography (EEG) recording. Each modality task started with the baseline phase, followed by the task phase and the subject's difficulty rating. Note: ISI= interstimulus interval.

components and high-frequency interferences like muscular artifacts. REBLINCA algorithm (Di Flumeri et al., 2016) was applied on the Fpz channel to eliminate eye-blink contributions without losing data. Specific procedures of the EEGLAB toolbox (Schwartz Foundation, Halesite, NY, USA) (Delorme and Makeig, 2004) were used to deplete the signal from other artefacts. The EEG dataset was segmented into epochs starting at 500 ms before stimulus onset and ending at 2500 ms after the offset. This temporal windowing was adopted to respect the condition of stationarity of the EEG signal and allow for a high number of observations for the number of variables considered in the analysis (Elul, 1969). To identify artefacts, three validated criteria according to published procedures (Cartocci et al., 2023a; Inguscio et al., 2022b) were employed: (i) threshold criterion ($\pm 80 \mu\text{V}$); (ii) trend estimation criterion (slope higher than $40 \mu\text{V/s}$ or less than $0.3 \mu\text{V/s}$); and (iii) sample-to-sample criterion (when, in terms of absolute amplitude, the signal sample-to-sample $>30 \mu\text{V/s}$). Finally, all epochs marked as 'artefacts' were removed from the EEG dataset, such that all analyses were based on clean EEG signals. Specifically, the percentage of artifacts removed in each group was as follows: NH group= 22.171%; UCI group= 31.704 %; BCI group= 35.258 %. Individual alpha frequency (IAF), given in Hertz, to accurately define EEG bands of interest, was computed for each participant on a 60 s long-closed eyes segment, recorded before the baseline phase (Klimesch, 1999). Each band was then defined as $\text{IAF} \pm x$, where x was an integer in the frequency domain; thus, the EEG signal was filtered in the following frequency bands in Hertz (Hz): theta [$\text{IAF} - 6 \div \text{IAF} - 2 \text{ Hz}$], alpha [$\text{IAF} - 2 \div \text{IAF} + 2 \text{ Hz}$], and gamma [$\text{IAF} + 16 \div \text{IAF} + 30 \text{ Hz}$] (Klimesch, 1999). Finally, the power spectral density (PSD) (Welch, 1967) was calculated for each epoch and channel, with a Hanning window of 1 s and an overlap of 500 ms. The topographical distribution of band modulation analysis was based on data averages for the following Areas of Interest (AOIs): frontal, parietal, occipital and hemisphere electrode locations. The channels considered were F3, F4, Fz (frontal); Pz, P3, P4, P7, P8 (parietal); O1, O2 (occipital); F3, C3, T7, P3, O1 (left hemisphere); F4, C4, T4, P4, O2 (right hemisphere). Of course, for the calculation of the AOIs for the left and right hemispheres, some channels were partially embedded in the calculation of other AOIs. However, autocorrelation risks were avoided because the correlation analysis between hemispheres and other AOIs was not performed.

To limit bias on scores due to subjective stimuli perception on VWM n-back task recording, before statistical analysis, PSD data were normalised subtracting the PSD calculated for the EEG signal acquired during the baseline phase of the audio and video tasks described above and also reported in Fig. 1 (Cohen, 2014).

2.5. Statistical

We tested the assumption of normality distribution for all variables (neurophysiological, linguistic and behavioural) using the Shapiro-Wilk normality test (Shapiro and Wilk, 1965) and the Levene test (Levene, 1960) to examine the assumption of variance of groups' equality. We could not use parametric ANOVA because most of the variables were not normally distributed, but the homogeneity assumption of the variance was met; therefore, the Kruskal-Wallis (KW) H test (Kruskal, 1952; Kruskal and Wallis, 1952) with a significance of $p = 0.05$ was used to test for any differences between the three independent samples for each dependent variable. The dependent variables considered were: receptive language results (PPVT); Performances (RTs; PE) n-back results for each n-back level (LOAD) (0,1,2) in each modality (MOD) of task (audio-AUD; video-VID); Alpha, Theta, and Gamma EEG activation in the AOIs considered for each LOAD in each MOD. Post hoc analysis was further conducted using Dunn's pairwise multiple comparisons with the Holm corrected significant p -value. The KW effect size was calculated with Epsilon Squared (\mathcal{E}^2) (Kelley, 1935) because it is a better choice than other tests when the sample size is small (Tomczak and Tomczak, 2014; Hays, 1978; Maxwell et al., 2017). Epsilon-Squared is also a more

conservative effect size estimate than the better-known eta-squared measure (Keppel, 1982).

Finally, nonparametric Spearman's correlation coefficient ρ was applied to measure the association between variables. Statistical analyses were performed using the computer software JASP (Version 0.17.2.1).

3. Results

3.1. Language results

The results of the Kruskal-Wallis test performed on the PPVT scores revealed significant differences between groups $H(2)=13.162, p = 0.001, \mathcal{E}^2 = 0.506$. Post hoc comparisons using the Dunn test with Holm corrections indicated that NH scores were observed to be significantly higher than those of group UCI ($p = 0.043$) and BCI ($p = 0.001$). The comparison between BCI and UCI groups was not significant ($p = 0.355$) (Fig. 2).

3.2. Behavioral results

Statistical analysis showed no significant differences between the three groups for reaction times for each n-back condition ($p > 0.05$).

Concerning performance during the visual task, no statistically significant differences emerged among the 3 groups ($p > 0.05$). Statistically significant results emerged in performance for the auditory task.

Indeed the KW test unveiled a group effect both for performance at level 2 during audio MOD H (2)=7.807, $p = 0.020, \mathcal{E}^2 = 0.323$ and considering overall performance at the auditory n-back $H(2)=10.580, p = 0.005, \mathcal{E}^2 = 0.438$. Pairwise comparisons using Dunn's test corrected indicated that in audio level 2 performance was significantly better for NH than UCI and BCI ($p = 0.048$ for both clinical groups), while no significant differences emerged between UCI and BCI ($p_{\text{BCI vs UCI}}=0.960$) (Fig. 3). Better performance persisted in NH compared to both UCI and BCI even when considering the entire audio task ($p_{\text{NH vs UCI}}=0.037$ and $p_{\text{NH vs BCI}}=0.007$); even in this condition, the two clinical groups did not differ from each other ($p_{\text{BCI vs UCI}}=0.649$) (Fig. 4).

3.3. EEG results

We constructed topoplots to visually represent the distribution of average PSD across the EEG scalp. Fig. 5 shows the topographic

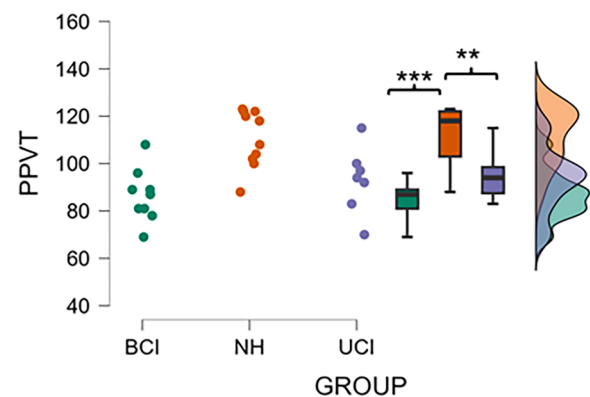


Fig. 2. Differences between groups (NH=Normal Hearing; UCI=Unilateral Cochlear Implant users; BCI=Bilateral Cochlear Implant users groups) for the Peabody Picture Vocabulary test (PPVT). Significant differences between groups emerging from post hoc test are indicated (** $p \leq 0.01$; *** $p \leq 0.001$). Data are shown as scatterplots, boxplots and raincloud plots. The thick lines in the middle of the box are the median; the box itself spans the range from the 25th percentile to the 75th percentile.

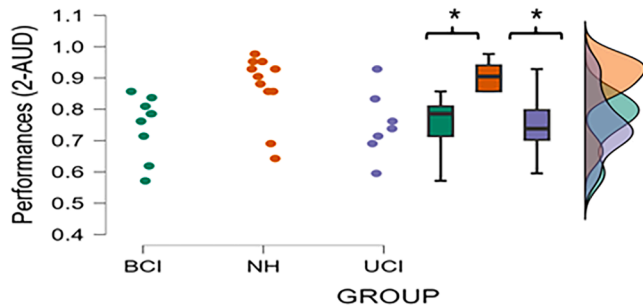


Fig. 3. Differences between groups (NH=Normal Hearing; UCI=Unilateral Cochlear Implant users; BCI=Bilateral Cochlear Implant users groups) in 2 audio n-back task performances. Significant differences between groups emerged from the post hoc test are indicated (* $p < 0.05$). Data are shown as scatterplots, boxplots and raincloud plots. The thick lines in the middle of the box are the median; the box itself spans the range from the 25th percentile to the 75th percentile.

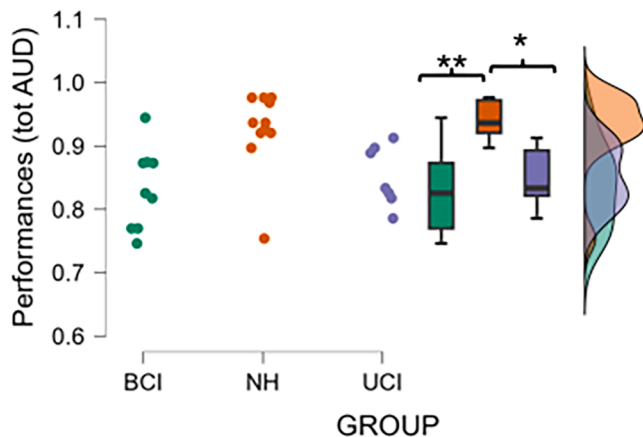


Fig. 4. Differences between groups (NH=Normal Hearing; UCI=Unilateral Cochlear Implant users; BCI=Bilateral Cochlear Implant users groups) in performances for total levels in the audio n-back task. Significant differences between groups emerged from the post hoc test are indicated (* $p < 0.05$; ** $p < 0.01$). Data are shown as scatterplots, boxplots and raincloud plots. The thick lines in the middle of the box are the median; the box itself spans the range from the 25th percentile to the 75th percentile.

configurations of theta (a), alpha (b) and gamma (c) activity calculated in each condition for the three groups.

Descriptively, the topoplots show globally for the BCI group similar electrocortical activities as for the NH group in the three bands considered. However, in the theta band the BCI group show more activity in the electrodes considered for the parietal and occipital temporal AOIs, especially for auditory modality. This pattern is also maintained in the gamma band for the auditory task, while in visual modality the activity increases during task difficulty in the occipital electrodes, in line with the control group. Alpha activity in the BCI group appears lower in the central areas than in the controls.

Considering the UCI group compared to the other two groups, an overall lower theta activity in all cortical areas, except in the temporal electrodes in the right hemisphere (particularly during the auditory task), clearly emerges from the topographic representation. Focusing on the gamma band, we again observe, when compared to the other two groups, greater diffuse activity on the electrodes placed on the right hemisphere (in particular for the auditory modality) and simultaneously lower activation with respect to the electrodes placed on the left hemisphere in addition to milder activity in the occipital areas in all conditions. With regard to the alpha band, it appears that the unilaterally implanted CI group have globally lower activity than the controls and

the bilaterally implanted children.

Regarding the statistical analysis performed on electrocortical activations during n-back audio and video, statistically significant results emerged for theta and gamma rhythms, while no significant results emerged for alpha rhythms ($p > 0.05$).

3.3.1. Theta results

Concerning theta activity in frontal AOI, the KV test indicated a significant difference between groups in the 2 audio conditions $H(2)=8.625, p = 0.013, \mathcal{E}^2=0.357$ and in the audio condition in total $H(2)=6.231, p = 0.044, \mathcal{E}^2=0.258$. Post hoc Dunn's test corrected revealed, for the first analysis, significantly less theta activity for UCIs compared with both NH ($p = 0.019$) and BCI ($p = 0.027$) while there was no statistically significant difference between the NH and BCI groups ($p = 0.872$) (Fig. 6). Considering the second analysis, the only significant difference was between UCI and BCI, in favour of the latter ($p = 0.040$), while no statistically significant difference was observable between BCI and NH groups ($p = 0.362$) and between UCI and NH groups ($p = 0.168$) (Fig. 7).

A difference in theta activity also emerges from the analysis conducted on the left hemisphere $H(2)=5.997, p = 0.050, \mathcal{E}^2=0.248$ (Fig. 8). Here, the post hoc shows less activity in UCI group than in BCI group ($p = 0.043$). No other differences between groups were statistically significant ($p = 0.280$).

3.3.2. Gamma results

Significant differences in electroencephalographic activity in the left hemisphere also emerged in the gamma band, where they are observed for the total audio task $H(2)=7.350, p = 0.025, \mathcal{E}^2=0.304$. The post hoc test shows less activity in the UCI group than in both the BCI and NH groups ($p = 0.041$ and $p = 0.041$, respectively), while the comparison between NH and BCI was not significant ($p = 0.998$) (Fig. 9).

A significant difference in the gamma band was also found in the parietal AOI in the total audio condition $H(2)=7.833, p = 0.020, \mathcal{E}^2=0.324$. Dunn's post hoc test corrected revealed significantly less intense activity in the UCI group in comparison with both NH ($p = 0.039$) and BCI ($p = 0.026$), while no statistically significant differences emerged between NH and BCI ($p = 0.671$) (Fig. 10).

Finally, also in occipital AOI, the KW test indicated significant differences between groups in gamma rhythm during the total audio condition $H(2)=10.002, p = 0.007, \mathcal{E}^2=0.414$. Dunn's post hoc test corrected revealed significantly less intense gamma rhythm in the UCI group in comparison with both NH ($p = 0.006$) and BCI ($p = 0.034$), while no statistically significant difference emerged between NH and BCI ($p = 0.526$) (Fig. 11).

3.4. Correlations between variables

The results from Spearman's correlation coefficient applied to investigate possible linear relationships between the variables showed some significance within the three groups.

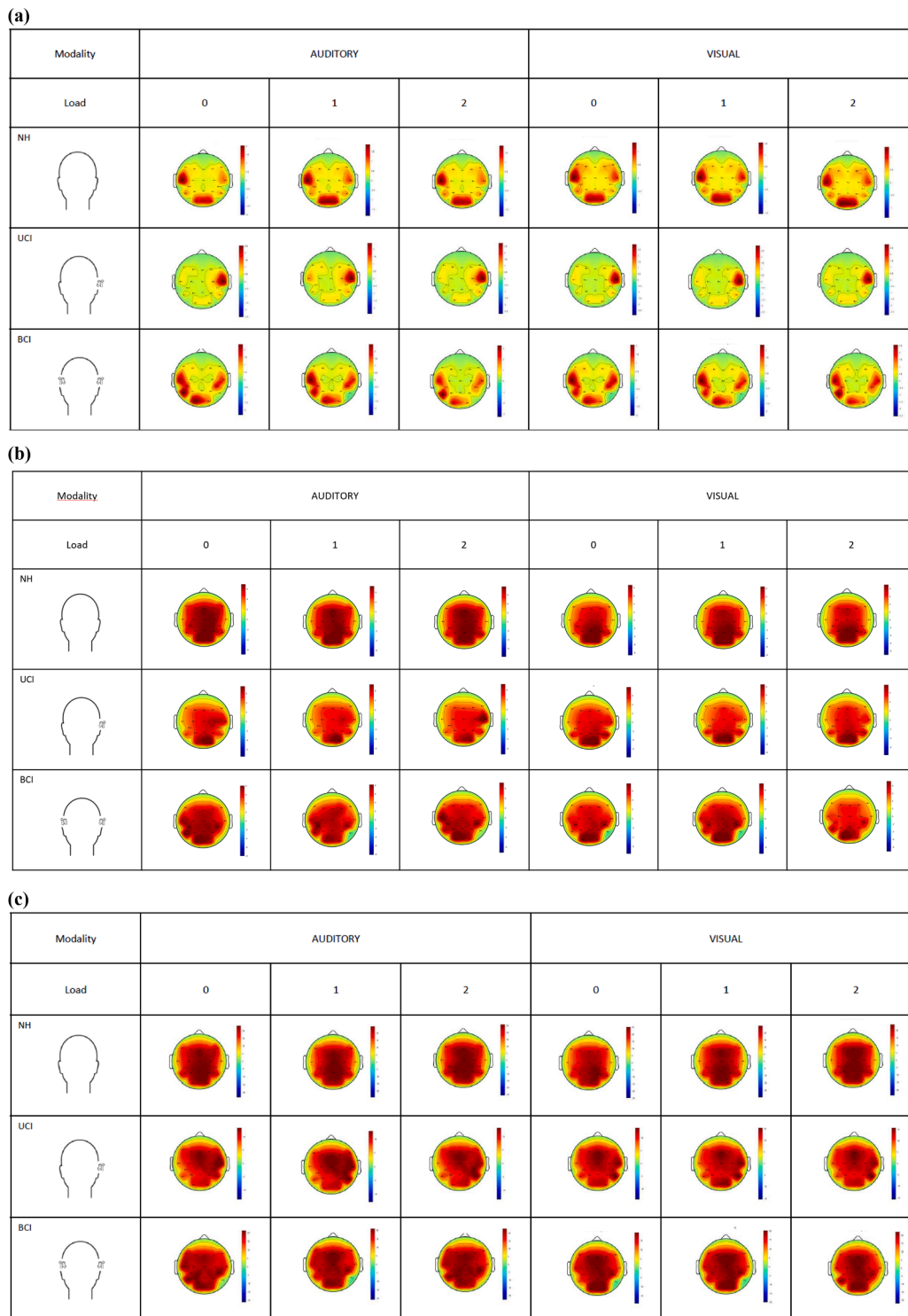
Within the NH group, a positive correlation is observed between audio performance and gamma activation in the left hemisphere and performance at the audio task ($\rho=0.664, p = 0.026$) (Fig. 12a) as well as a correlation between PPVT score and chronological age ($\rho=0.743, p = 0.009$) (Fig. 12b).

Within the BCI group we also found a relationship between left hemispheric gamma activation and performances at the audio task ($\rho=0.698, p = 0.037$) (Fig. 13)

Within the UCI group, on the other hand, frontal theta activity correlated with performance for the auditory task $\rho=0.821, p = 0.034$ (Fig. 14a). Furthermore, a relationship was observed between gamma activation in parietal AOI and age ($\rho = 0.811, p = 0.027$) (Fig. 14b).

4. Discussion

In the present study, we investigated the behavioural and neural



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Fig. 5. Scalp distributions of the Electroencephalographic (EEG) (a) theta, (b) alpha and (c) gamma spectral power respectively during the audio and video n-back tasks. For each group (NH=normal hearing; UCI=unilateral cochlear implant users; BCI=bilateral cochlear implant users) from left to right, the scalp maps correspond to the sensorial Modality (auditory; visual) and Load (0, 1, 2 level) of the n-back verbal working memory (VWM) task conditions. The black dots correspond to the positioning of the 20 electrodes positions according to 10–20 international system. Red indicates a higher PSD while blue indicates a lower PSD.

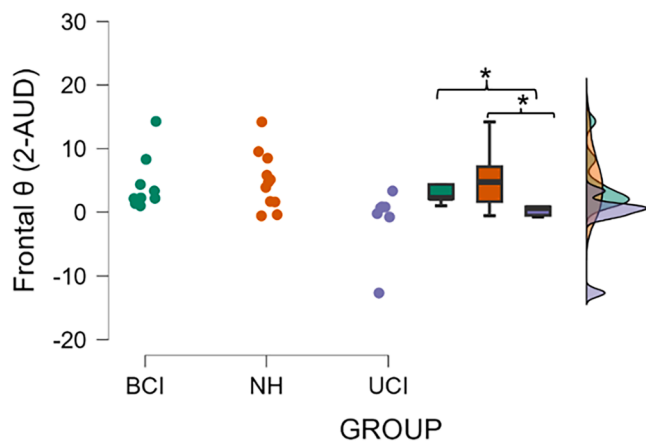


Fig. 6. Theta (θ) band activity. The figure shows the differences between groups (NH=Normal Hearing; UCI=Unilateral Cochlear Implant users; BCI=Bilateral Cochlear Implant users groups) for theta activation in the frontal area of interest during 2 audio n-back task conditions. Significant differences between groups emerging from post hoc test are indicated ($*p \leq 0.05$). Data are shown as scatterplots, boxplots and raincloud plots. The thick lines in the middle of the box are the median; the box itself spans the range from the 25th percentile to the 75th percentile.

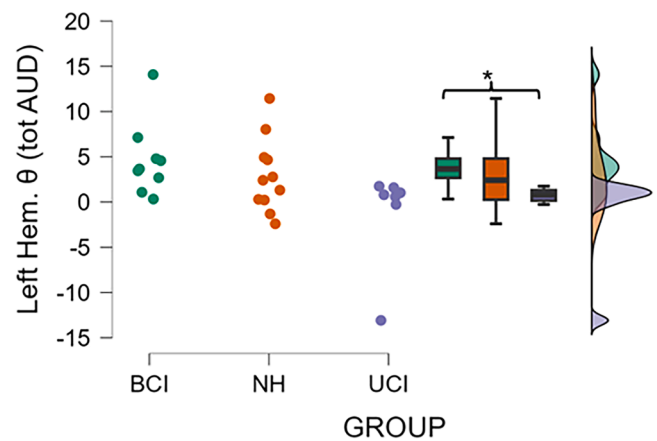


Fig. 8. Theta (θ) band activity. The figure shows the differences between groups (NH=Normal Hearing; UCI=Unilateral Cochlear Implant users; BCI=Bilateral Cochlear Implant users groups) for theta activation in the left hemisphere area of interest during total audio n-back task condition. Significant differences between groups emerging from post hoc test are indicated ($*p \leq 0.05$). Data are shown as scatterplots, boxplots and raincloud plots. The thick lines in the middle of the box are the median; the box itself spans the range from the 25th percentile to the 75th percentile.

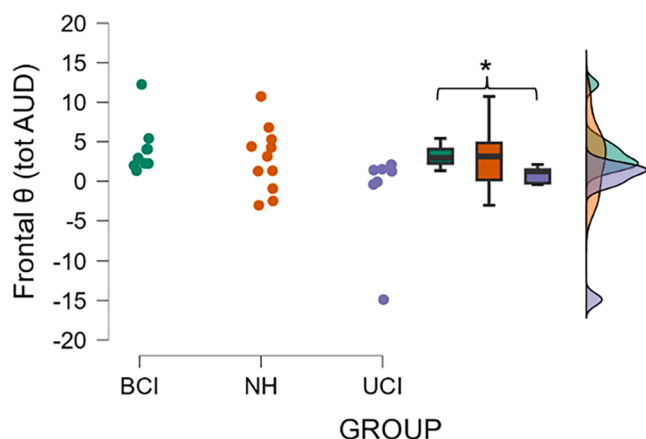


Fig. 7. Theta (θ) band activity. The figure shows the differences between groups (NH=Normal Hearing; UCI=Unilateral Cochlear Implant users; BCI=Bilateral Cochlear Implant users groups) for theta activation in the frontal area of interest during total audio n-back task condition. Significant differences between groups emerging from post hoc test are indicated ($*p \leq 0.05$). Data are shown as scatterplots, boxplots and raincloud plots. The thick lines in the middle of the box are the median; the box itself spans the range from the 25th percentile to the 75th percentile.

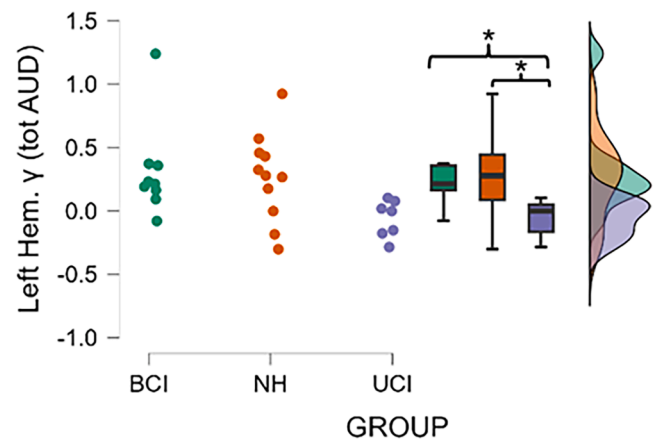


Fig. 9. Gamma (γ) band activity. The figure shows the differences between groups (NH=Normal Hearing; UCI=Unilateral Cochlear Implant users; BCI=Bilateral Cochlear Implant users groups) for gamma activation in the left hemisphere area of interest during total audio n-back task condition. Significant differences between groups emerging from post hoc test are indicated ($*p \leq 0.05$). Data are shown as scatterplots, boxplots and raincloud plots. The thick lines in the middle of the box are the median; the box itself spans the range from the 25th percentile to the 75th percentile.

correlates of VWM processing during an auditory n-back task and a visual n-back task by comparing three groups of children with different auditory characteristics: normal hearing, unilateral and bilateral CI users. While these measurements have already been carried out for visual WM tasks in groups of hearing adults and children (Jaeggi et al., 2010; Yapple and Arsalidou, 2018; Pesonen et al., 2007; Palomäki et al., 2012), no study to date has simultaneously investigated the performance and cerebral cortical activations occurring during VWM tasks in two sensory modalities (auditory and visual) comparing children with different hearing experiences. The main purpose was to investigate differences in VWM performance between unilaterally and bilaterally implanted children by exploring whether EEG patterns could reveal underlying neurophysiological factors for the WM deficits found in CI children compared with NH peers, thus providing hypothetical brain-based causes for the extreme variability found in clinics and

rehabilitation settings for the same CI users.

4.1. Language outcomes

In receptive vocabulary, NH children achieve better outcomes than peers with CI (Fig. 2), confirming the risk of delays in receptive vocabulary development acquisition in CI users, as reported in several studies assessing oral language skills in the CI population (El-Hakim et al., 2001; Fagan and Pisoni, 2010; Herran et al., 2023). Moreover, a positive correlation of receptive vocabulary with chronological age was only found in the NH group (Fig. 12.b), which is consistent with evidence showing that vocabulary, in children without language difficulties, correlates significantly with more advanced levels of schooling (Rosselli et al., 2014). In fact, the NH group was not characterized by the same schooling level, (see Table 1) a factor that may have affected, in

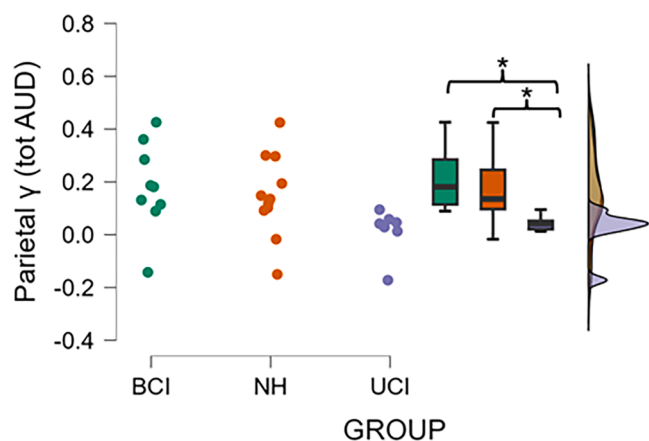


Fig. 10. Gamma (γ) band activity. The figure shows the differences between groups (NH=Normal Hearing; UCI=Unilateral Cochlear Implant users; BCI=Bilateral Cochlear Implant users groups) for gamma activity in the parietal area of interest during total audio n-back task condition. Significant differences between groups emerging from post hoc test are indicated ($*p \leq 0.05$). Data are shown as scatterplots, boxplots and raincloud plots. The thick lines in the middle of the box are the median; the box itself spans the range from the 25th percentile to the 75th percentile.

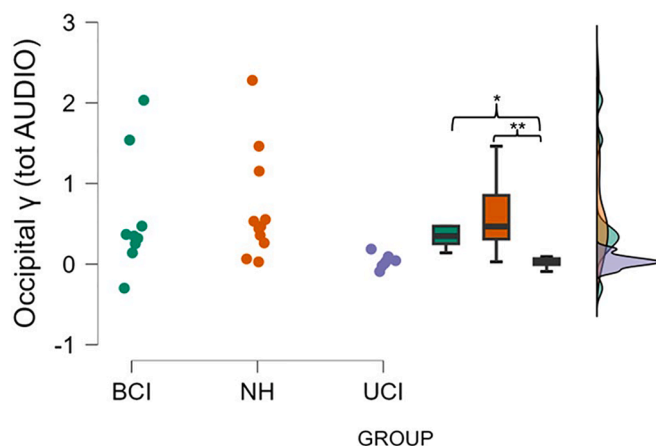


Fig. 11. Gamma (γ) band activity. The figure shows the differences between groups (NH=Normal Hearing; UCI=Unilateral Cochlear Implant users; BCI=Bilateral Cochlear Implant users groups) for gamma activity in the occipital area of interest during total audio n-back task condition. Significant differences between groups emerging from post hoc test are indicated ($*p \leq 0.05$; $**p \leq 0.01$). Data are shown as scatterplots, boxplots and raincloud plots. The thick lines in the middle of the box are the median; the box itself spans the range from the 25th percentile to the 75th percentile.

addition to age, the correlation we found. In addition, language development during school years, is closely related to the development of other non-linguistic skills including individual and family characteristics (Gibson and Petersen, 2010; Armstrong et al., 2016) that were not explored in further detail as they were outside of the focus of the present study.

Furthermore, we did not find any significant differences between clinical groups, when comparing lexical comprehension levels attained by unilaterally or bilaterally implanted children, assessed through the PPVT test. Although other authors including (Sarant et al., 2014), when using the same test, reported a significant difference in vocabulary comprehension, the potential beneficial effect of bilateral hearing in the present study could be covered by some important variables— such as parenting style (Quittner et al., 2013; Sarant et al., 2009), presence of siblings (Barton and Tomasello, 1994), cultural and socioeconomic

(Piccolo et al., 2016; Ribeiro et al., 2023) family background (Niparko et al., 2010; Cutting and Dunn, 1999)—that were not possible to account for, due to our relatively small sample size. However, we controlled the analysis for variables predictive of language performance—such as chronological age (Campbell, 1998), age at implantation (Geers et al., 2009; Schorr et al., 2008), non-verbal IQ (Phillips et al., 2014; Cejas et al., 2018) and presence of neuropsychiatric disorders. Thus, the contribution of one or two CIs to receptive language performance could also be affected by other factors, which were not investigated as they were not the subject of the present study.

4.2. Behavioural results

In line with several previous studies on VWM (Burkholder and Pisoni, 2003; AuBuchon et al., 2019; Romano et al., 2021), performance at n-back is affected by cochlear implantation, both unilaterally and bilaterally during the auditory tasks when considering average performances (Fig. 4) and considering the most difficult auditory level (n2) (Fig. 3), as found by Nittrouer et al. (2017) for auditory VWM tasks and by Pisoni and Cleary (2004) in the visual-auditory VWM comparison. Our findings were as expected, given that DHH children using CI have previously been found to have shorter digit spans (Burkholder and Pisoni, 2003); however, they do differ from previous studies of our group (Inguscio et al., 2022a) that showed no significantly worse performance at auditory tasks for UCI children. The difference in performance from the previous sample of UCI that we investigated could be due to intervening variables not previously considered and the statistical methods used. Globally, behavioural VWM performances significantly differed between CI users and hearing controls only during the processing of auditory stimuli. Interestingly, there are no differences between groups regarding the level of task difficulty alone (0;1;2 back). It would therefore appear that degraded performance is related to sensory rather than cognitive processing difficulties (Pisoni et al., 2017). Indeed, the absence of differences between clinical and control groups suggests that the difficulty is due precisely to sensory modality rather than VWM per se.

Although we did not assess phonology in participants, the ‘phonological bottleneck hypothesis’ could contribute to understanding our results in auditory VWM performance in the clinical groups. This term was originally coined for studies of VWM in children with dyslexia (Shankweiler et al., 1979, for a discussion review Caylak, E. 2010; Knoop-van Campen et al., 2018), and suggests that WM deficits in children with CI originate primarily from poor ‘phonological awareness’ (PA). PA skills, tapped by tasks requiring the manipulation of phonological structure (Gathercole et al., 2006), refer to the recognition of the structure states of heard or read language such as syllables, rhymes and single phonemes. The latter are most pertinent to the objective of the present study, as they are related to VWM. In fact, as Nittrouer et al., observe (2017), several studies on CI users have found more significant phonological deficits than deficits for other syntactic and lexical skills (see, for example, Nittrouer and Caldwell-Tarr, 2016; Ambrose et al., 2012; Spencer and Tomblin, 2009). Moreover, studies suggested that performance on VWM tasks in CI users could be partly due to fragile, underspecified phonological representations of letters in short-term memory (Pisoni et al., 2011) and that PA plays a crucial role in reading development in the lower grades of primary education (Anthony and Francis, 2005). Such evidence could suggest that PA deficits can be due to the degraded representation of the auditory signal that children with CI must rely on due to CI processing limitations in the spectral domain. In fact, while the sensitivity between children with and without CI is shown to be similar for temporal and amplitude elements indicating phonemic categories, there is a decrease in sensitivity to spectral stimuli (Moberly et al., 2016). Consequently, an additional interpretative hypothesis of our findings might be that the processing of the spectral component of listening in the n-back stimuli, does not vary between use of one or two CI. However, to confirm this interpretative key, a thorough

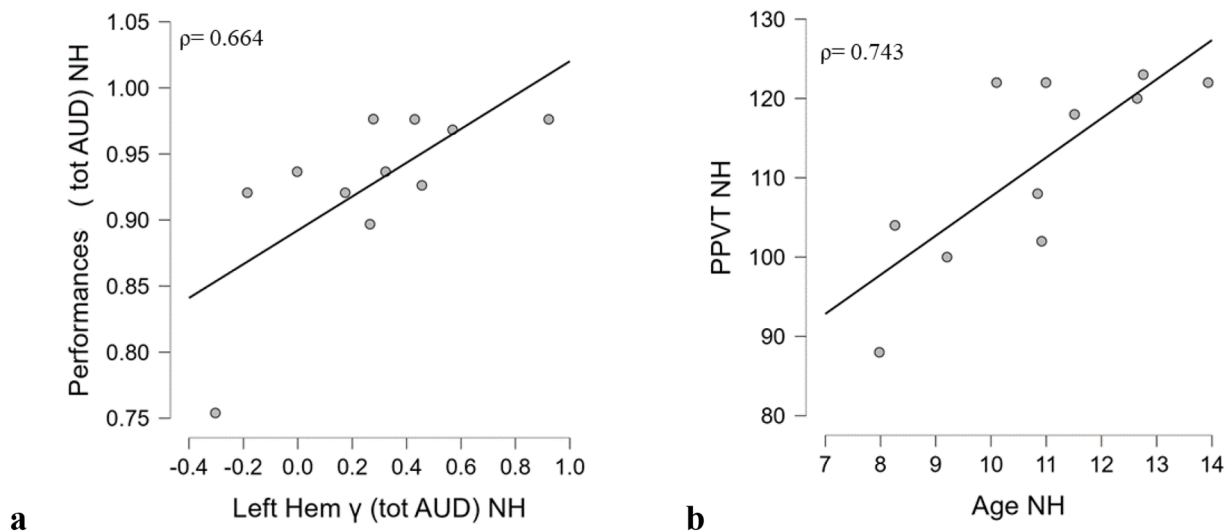


Fig. 12. The relationship between variables in NH. (a) Scatter plot showing a positive correlation between performances and gamma activation in left hemisphere (Hem) AOI for audio task. (b) Scatter plot showing a positive correlation between the Peabody picture vocabulary test (PPVT) and chronological Age. *Note:* NH=normal hearing group; AOI=Area of Interest; AUD= audio.

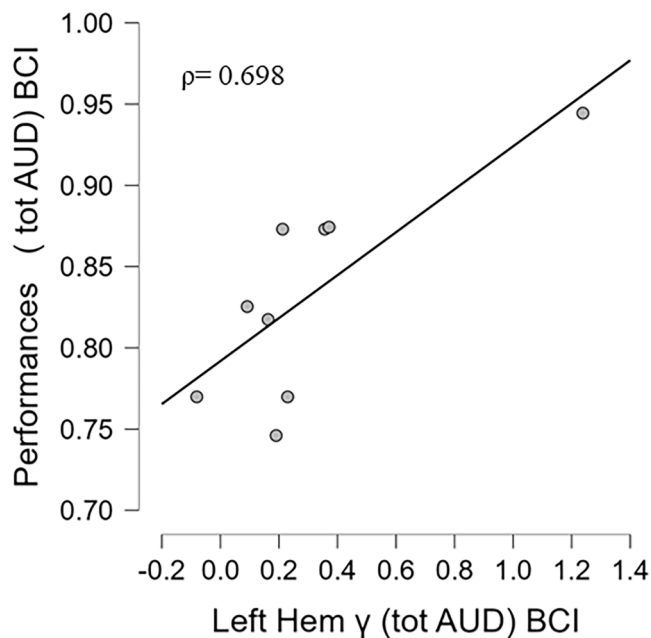


Fig. 13. The relationship between variables in BCI. Scatter plot showing a positive correlation between performances and gamma activation in the left hemisphere (Hem) AOI for audio task. *Note:* BCI=bilateral cochlear implant group; AOI=Area of Interest; AUD= audio.

audiological study of the type of processor used by patients (Table 1) would be appropriate in relation to the spectral analysis of the auditory stimuli used in the protocol. Finally, the absence of differences between UCI and BCI in performance should be evaluated in light of the EEG results discussed below.

4.3. EEG results

Considering cortical power spectral density analysis based on electrode distribution, differences are observed between groups in theta band (Fig. 5.a) and gamma band (Fig. 5.b). Statistically significant electrocortical differences will be discussed below.

4.3.1. Theta band

The present results contrast with our previous study that showed no difference between NH and UCI in frontal theta AOI during VWM tasks (Inguscio et al., 2022a). In fact, here we observe significantly less theta activity in UCI than in BCI for the total audio condition (Fig. 7) but also significantly less activity when compared to both BCI and NH regarding the hardest audio condition (Fig. 6). The results suggest a lack of attention in UCI during the (supposed) hardest (for DHH people) VWM condition in line with studies which observed increasing attention in correspondence to the experimental situation characterised by higher memory load and/or effortful cognitive processes in hearing controls (Wisniewski et al., 2018).

Moreover, the frontal deactivation in the theta band could be a sign of decreased attentional resource allocation availability due to the perceived LE (Cartocci et al., 2018; 2023b) experienced during the auditory VWM task solely by UCI compared to BCI. Indeed, mirroring that which was observed and proposed by Wisniewski et al. (2018) on frontal activation in theta as a sign of LE— frontal theta collapse in the UCI group could reflect a VWM component of effortful listening (cf. Pesonen et al., 2006). Furthermore, considering the self-report measures showing that the most challenging task was the auditory task for 42.85 % of UCI compared to 77.77 % of BCI and 54.54 % of NH, it becomes clear that UCI users explicitly underestimate the difficulty in the auditory tasks while implicit neurophysiological markers and behavioural performance suggests the opposite.

Globally, we might speculate that in the framework of Kahneman's consolidated capacity-constrained resource model (Kahneman, 1973), a frontal 'theta deactivation' could reflect a withdrawal from cognitive engagement (i.e. a fatigue condition due to unsustainable, prolonged LE). In fact, the auditory n-back task for CI users could actually be considered a near-simultaneous (auditory attention to the stimulus and unfolding of the n-back) dual task (Perreau et al., 2017). Consequently, the differences we found could be explained by the different tasks required in the experimental protocols. Our interpretive hypothesis about the frontal activation deficit in theta caused by the auditory condition could be further validated by the fact that in the n-back, the listening did not occur in the noise. Therefore, less theta activity in frontal AOI in the UCI group could be indicative of a subtraction of brain resources to the cognitive task because of the increased difficulty in the n-back auditory task due to the listening conditions for this clinical group. Thus, is it the lack of cognitive resources in the UCI group due to fatigue related to the auditory stimulation modality that worsens

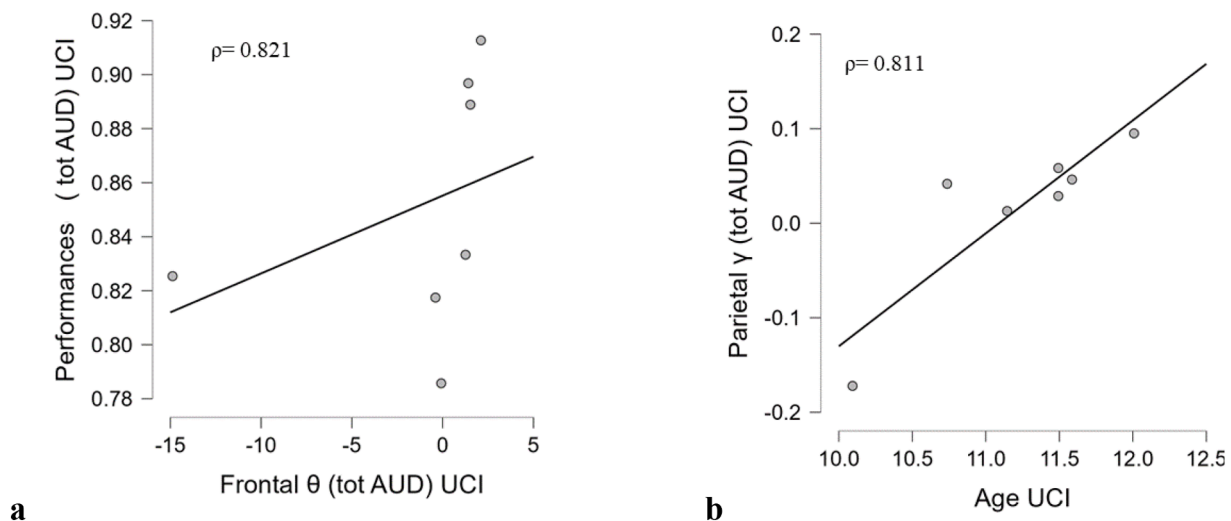


Fig. 14. The relationship between variables in UCI. (a) Scatter plot showing a positive correlation between performances and theta activation in frontal AOI for audio n-back task condition. (b) Scatter plot showing a positive correlation between chronological age and electrocortical gamma activation in parietal AOI during audio n-back conditions *Note:* UCI=unilateral cochlear implant group; AOI=Area of Interest; AUD= audio.

performance? This hypothesis seems confirmed by the positive, strong correlation observed in UCI between PE audio and frontal theta audio (Fig. 14.a). Finally, these significant results, also considering the absence of differences between BCI and NH controls, suggests that there is a neurophysiological benefit conferred by bilateral implantation in the auditory processing of VWM.

Concerning our results on theta power between UCI and BCI in left hemisphere AOI (Fig. 8). It is often assumed that the functional lateralisation of the human brain has an adaptive value and may even present a prerequisite for the full realisation of linguistic potential (Knecht et al., 2001). In addition, neuroimaging studies (Nagel et al., 2013) suggest left hemispheric lateralisation in VWM tasks and right hemispheric lateralisation in spatial WM tasks. Moreover, the laterality effect is consistent with extensive neuropsychological and neuroimaging studies suggesting that verbal tasks, including VWM tasks, predominantly implicate left hemisphere activity (Yao et al., 2023; Emch et al., 2019; Owen et al., 2005). Furthermore, results from language development studies have suggested that the brain plasticity mechanisms involved in language learning are different from those recruited later for automated, skilled language (Stiles et al., 1999). As Spironelli and colleagues highlighted (2010), the achievement of the typical left hemisphere specialisation for linguistic functioning can only be attained once earlier critical stages of learning are completed. Moreover, typical lateralisation also seems to require linguistic input during the critical period for language acquisition: if language learning happens outside of the critical period, cerebral asymmetry may not be fully established (Martin et al., 2022). Thus, early profound congenital deafness may also alter the pattern of cerebral asymmetry for language that has been shown to favour the left hemisphere in the first months of life in typically developing infants with normal hearing (Dubois et al., 2009). We report this body of evidence to emphasise how hemispheric asymmetry reflects a fundamental principle of neuronal organisation and plays a critical role in children's motor, sensorimotor, and cognitive development (Babik, 2023) and that the achievement of left hemispheric specialisation for language functioning can only be achieved when critical *early* levels of learning are obtained. Moreover, even at the *sensory* level, functional asymmetry seems to be an established feature of the functional organisation of the human brain (Geschwind and Galaburda, 1985). For example, verbal sound processing occurs predominantly in the left hemisphere, while nonverbal sound processing predominates in the right hemisphere (Tervaniemi and Hugdahl, 2003). Furthermore, concerning effective communication between different brain regions involved in language processing, theta

band activity has been shown to be critical in association with better VWM capacity (Wu et al., 2007; Sauseng et al., 2010; Jausovec and Jausovec, 2014; Koirala et al., 2023) acting as an interface for language and memory (Pu et al., 2020).

Based on the reported scientific evidence, the significant theta rhythm differences found in the left hemisphere during all of the auditory conditions for the UCI group compared to the BCI group (Fig. 8), could be interpreted as a reduction in left hemisphere activity as a result of language depletion due to unilateral cochlear implantation as found in neurophysiological studies with NH (Bidelman and Howell, 2016). Interestingly, theta activity in UCI's left hemisphere aligns with the deficits found in verbal tasks in children with dyslexia. Such difficulty in processing the underlying phonological structure of speech may be associated with disruption of the left hemisphere language network (Spironelli et al., 2008). Indeed, several studies have linked the phonological disorders observed in dyslexic children to VWM deficits (Ramus et al., 2003; 2004), while the neurophysiological findings of Spironelli et al. (2006, 2010) suggest that theta oscillation in the left hemisphere may be considered a marker of the phonological deficit found in children with dyslexia.

Based on our data, we can very cautiously advance the hypothesis — concerning children with CI frequently having a PA deficit (Werfel and Hendricks, 2023) — that the differences in theta rhythms in the left hemisphere between UCI and BCI could be a neurophysiological marker of a PA deficit in children with CI also shared by other children with atypical development such as dyslexic. Moreover, this theta-EEG pattern could be specifically connected to their performances since, for UCI, theta activity in frontal areas is strongly correlated with performance (Fig. 14.a). It could be hypothesised that for UCI children, the hypoactivation of theta related to poor PA fails to support a left-hemispheric network that manifests in a frontal deactivation (Fig. 7) and, thus, resulting in poor performance. Furthermore, delving more deeply into the phonological characteristics of deafness, in accordance with the 'lexical restructuring model', phonological representations initially form holistically and then gradually segment into forms along with children's increasing number of lexical entries (Metsala and Walley, 1998). In fact, the majority of evidence suggests that children's phonological awareness develops sequentially, beginning with a shallow sensitivity to large phonological units (e.g. syllables) and proceeds towards a deep awareness of small phonological units (e.g. phonemes) (Kim, 2008), although this is not without debate (Carroll et al., 2003). Subsequently, phonological representation is continually shaped and synchronised by

continuous exposure to the sounds and structures of language perceived in the environment (Zhang et al., 2022). It is not surprising, therefore, that DHH children constantly struggle when forming phonological representations for specific problems in phonological memory and phonological sensitivity (Ingvalson et al., 2020). Moreover, as Zhang (2022) notes, the stability and maturity of phonological representations are closely related to PA skills, considering how memory (specifically working memory) contains the phonological structure of specific words and their constituent segments. Thus, the deficits observed in UCI children in PA (Lund, 2020; Lee, 2020; 2012) could be caused by low phonological representation due to auditory deprivation or brief auditory experience, in line with a (delayed) developmental trajectory.

The illustrated literature, also taking into consideration a recent review summarizing neural correlates of PA (Stekić et al., 2023), could tentatively support our hypothesis of the left hemispheric theta hypoactivation found in UCI as a marker of PA deficits and, therefore, the possible cause of auditory VWM deficits in this group.

Furthermore, Lee (2020) observed that age at implantation and receptive lexical skills influenced the development of PA skills in children with monolateral CI. We did not find these correlations in UCI, but this could be because Lee et al. (2012) compared early and late implanted CI users to NH. Our UCI participants were implanted early (Table 1) and, as anticipated in the introduction, were homogeneous in auditory age so that they might be aligned with NH for these variables.

However, as far as left hemisphere lateralization is concerned, the similarity between unilaterally implanted children and dyslexic children is not very strong, and further studies with comparisons made between more numerous and disparate clinical groups (children with unilateral, bilateral cochlear implantation and with dyslexia) and variables (e.g., in-depth phonological assessments and learning disabilities), might confirm this first interpretative hypothesis. Our findings, indeed, although limited, strongly point towards the need to investigate the neurophysiological correlates of phonology in children with CI.

An additional, stronger interpretative hypothesis on the lower activation of theta in UCI, is that based on the ‘maladaptive plasticity theory’ proposed by Gordon et al. (2013). Indeed our result, showing lower theta activity in AOIs located in the left hemisphere in the UCI group (noting that all were with right side implants) corroborates the evidence that asymmetric hearing in early life promotes greater representation of the better ear (or single ear in the case of single side deafness - SSD) in auditory and associative cortices (for review, Gordon and Kral 2019). In fact, unilateral hearing in childhood restricts input along the bilateral auditory pathways, possibly causing permanent reorganization (Gordon et al., 2015) Notably, as Lee et al. (2020) point out, cortical reorganization driven by unilateral hearing can occur throughout childhood and cortical preference for the stimulated ear persists even in children who received bilateral CI with delays greater than 2–3 years (Gordon et al., 2013): the asymmetry of auditory input in these cohorts is similar to that found in children with SSD. In the light of this evidence, it could be surmised that the continued use of CI promotes the strengthening of pathways through the cochlear-implanted ear, but did not protect them from the onset of continued impairment due to the deaf ear pathways.

Our results, discussed in line with the reported scientific evidence, and supported by the two interpretative advanced hypotheses above could suggest *firstly* that bilateral implantation grants the child an advantage in PA skills. This might explain the variability in VWM tasks among implanted children in light of the relationship between phonological detection and WM tasks. A thorough assessment of participants’ phonological skills could further support this interpretation of the neurophysiological results. Furthermore, the twofold difference found in the activation of theta (frontal and left hemispheric) in the UCI group could be a sign of an hypo-brain activation network underlying the processing of the auditory VWM. We advance this inference in the light of the left supramarginal gyrus’s dual involvement in WM and phonological processing (Paulesu et al., 1993; Ravizza et al., 2004; Østby et al., 2011). However, we clearly cannot draw any hasty conclusions as we

have not conducted a connectivity analysis.

Secondly, based on the maladaptive plasticity theory, the asymmetric cortical reorganization in unilaterally implanted children could be a possible cause of poor performance at the auditory VWM task.

4.3.2. Gamma band

Considering the *sensory information* underlying *brain function*, a peculiarity of the human nervous system is that each cerebral hemisphere receives information mainly from the opposite half of the body (Kimura, 1973). Moreover, it has been accepted that auditory signals are predominantly processed by the contralateral auditory cortex in typical hearing individuals (Gutschalk and Steinmann, 2015; Schönwiesner et al., 2007). In fact, although the auditory cortex receives sensory input from both ears, there is a large corpus of functional imaging, electrophysiologic, and behavioural data showing that it is most excited by stimulation of the contralateral ear (Langers et al., 2005). Furthermore, the effect of the side of implantation on behavioural performance in prelingually deafened children with CI is not yet known. Preliminary results in a small group of children indicated that, whereas behavioural speech perception performance in children with right versus left CI was comparable, their brain activation patterns differed (Henkin et al., 2008).

Therefore, since the auditory system is predominantly crossed, the neural input from the right ear to the left cerebral hemisphere should be stronger than that from the right ear to the right cerebral hemisphere. And, since the left hemisphere usually contains the neural system for speech perception (Kimura, 1973), it is reasonable to assume that speech sounds presented to the right ear have more access to the speech perception system. Furthermore, there is confirmation in the literature of a ‘right cochlear implant advantage’ over the left in speech perception in preverbal deaf children (Henkin et al., 2008), while, as anticipated in the introduction, numerous studies observed the involvement of the gamma band in the perception and maintenance of WM (Jokisch and Jensen, 2007; Tallon-Baudry et al., 1998; Howard et al., 2003).

The statistically significant reduced power of the gamma band in UCI compared to BCI and NH in the left hemisphere (Fig. 9) and in parietal AOIs (Fig. 10), in addition to confirming previous results of our research group (Inguscio et al., 2022a; Cartocci et al., 2021), would seem to suggest firstly a ‘non-advantage’ in having right sided CI with regard to the development of VWM for unilateral patients (Table 1), and secondly, there is a deficit in the processing of auditory stimuli considering that the parietal cortex plays a role in the network that integrates auditory features for perceptual judgments (Yao et al., 2020) and its involvement in the storage of verbal material in WM tasks (Jonides et al., 1998).

Moreover considering that parietal lobes have traditionally been considered ‘association cortex,’ where information from separate sensory processing pathways is combined to form a unified sensory space (Andersen, 1997), our findings in parietal AOI (Fig. 10) together with those in occipital AOI (Fig. 11) during the auditory task (carried out with eyes open at the PC), could suggest in unilaterally implanted children a poor interaction between parietal and primary sensory areas (Innes-Brown et al., 2013). Furthermore, consistent with Zhang’s (2023) study, it appears that in children with unilateral implants the visual cortex (occipital lobe) decreases its activity probably to allocate more resources when responding to auditory stimuli. Therefore, the visual cortex might support-rather than hinder-the activity of the auditory cortex (deficient due to auditory deprivation) during the auditory VWM task, and this phenomenon might be one of the elements that allows the UCI group to maintain the same performance at this task when compared with the BCI group (Figs. 3; 4). However, we did not find a correlation between behavioural outcomes and gamma activity in occipital AOI. Furthermore, the differences we observed for UCI in comparison with BCI and NH in the parietal and occipital areas would seem to show that in multimodal tasks of complex executive functions such as VWM, the auditory and visual systems must support each other rather than compete. Notwithstanding this, unilateral CI users showed differing EEG

activity patterns in auditory VWM tasks in sensory cortices that could point to reorganization in both auditory and visual cortices (Chen et al., 2016) that could suggest a neurophysiological cause for WM difficulties in children with CI.

Additionally, our findings seem to suggest that right side implantation does not fully complete the contralateral and parietal cortical developments that are fundamental for good performance in VWM n-back tasks. Support for this assumption is provided by the significant correlations found between left hemispheric activity in gamma and the performance in auditory VWM in BCI, (Fig. 13) as well as in NH (Fig. 12.a). Clearly, this interpretative hypothesis can only be confirmed by comparing these results with children who have left-sided implantation. We can state here, however, that the unilateral right-side implant could be deficient in supporting the gamma cortical configuration connected with performances during auditory n-back tasks shown by NH children and bilaterally implanted children. This deficit seems to be supported by the existing relationship between activation in parietal AOI and chronological age in UCI (Fig. 14.b), which suggests that UCI children still need to reach a neurophysiological cortical maturation *plateau* in associative areas before they can develop a neurophysiological strategy supporting performances in line with NH despite having a (not statistically significant) higher mean age than the other two groups. Thus, although the performances in the VWM task in auditory modality are lower in implanted children compared to NH but without significant differences between those with one or two implants, the underlying neurophysiological patterns show significantly greater differences between UCI and both NH and BCI, suggesting a more immediate electrophysiological alignment to the VWM benchmark of NH in the bilateral group when compared to the unilateral group.

Finally, looking globally at the results, although no differences in mnemonic (Figs. 3; 4) and linguistic (Fig. 2) performances were observed between the two clinical groups, there were with respect to the control group, and the EEG analysis has allowed us to highlight substantial differences between the two clinical groups. How advanced is essential because it opens up a new perspective in our understanding of VWM performance in DHH children that, although not differentiable between UCI and BCI, results from significant differences in cortical activation.

5. Conclusion

The present study was conducted to explore whether brain electroencephalographic responses can provide quantitative data on the cognitive VWM deficits present in children with CI and whether bilateral implantation results in improved VWM processing compared with unilateral implantation.

Through a bi-sensory neurocognitive approach, our results showed significant modality-dependent differences in EEG patterns during auditory VWM between children with and without CI. We generally observed cortical hypoactivation for UCI users in AOI (frontal, parietal, left hemispheric) critical for VWM abilities. In contrast, BCI users showed EEG patterns not significantly different from NH, suggesting attainment of the 'VWM's benchmark' of typical auditory development (Inguscio et al., 2021). According to these results, restoring bilaterality is critical for developing neurophysiological support for VWM.

Finally, it is worth emphasising how the role of cognition in speech perception has been increasingly explored in hearing research, with growing evidence that WM measures may provide additional clinical guidance for the selection of rehabilitation programs (Hillyer et al., 2019). Indeed, WM scores may be more sensitive to change and more effective in assessing benefits following CI application than traditional speech tests, considering that ceiling effects on speech perception are a growing clinical phenomenon in CI users (Gifford et al., 2008). While the assessment of cognitive abilities in CI users may shed light on why some patients achieve better speech outcomes, considering the wide variability found in cognitive functions such as WM, the assessment of the underlying neurophysiological patterns of VWM that emerged from

our study could provide clinicians with a means to better select and counsel patients on rehabilitation interventions.

Therefore, our findings may provide support for both the clinical diagnosis and rehabilitation programmes of DHH children, opening up new neuroscience-based multidisciplinary approaches in assisting the developmental pathway of children with cochlear implants.

6. Limitations and future directions

Our study, innovative as it is, has its limitations. Although our sample is not atypical in the CI literature (Kronenberger et al., 2011; Noble et al., 2023; Chitgar et al., 2023), it is relatively small, which may have limited our ability to detect minor differences. In addition, it would be interesting to add other tests on language skills and parental questionnaires to the methodology to consider the impact of the family environment on the neurocognitive development of the child with cochlear implantation (Holt et al., 2013). Thus, with a larger sample size, we could confirm the emerging evidence and further investigate the relationships between auditory, social-cognitive, and neurophysiological variables.

Finally, the next steps in approaching the investigated neurophysiological data could be to apply, in addition to power spectral density analysis a cross-frequency coupling analysis, (for a review Canolty and Knight, 2010; Kronenberger et al., 2018) to evaluate the interaction between brain oscillations on different frequency bands during working memory processing (Abubaker et al., 2021).

CRedit authorship contribution statement

Bianca Maria Serena Inguscio: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization. **Giulia Cartocci:** Conceptualization, Methodology, Validation, Writing – review & editing. **Nicolina Sciaraffa:** Software. **Maria Nicastrì:** Resources. **Ilaria Giallini:** Resources. **Pietro Aricò:** Software. **Antonio Greco:** Supervision. **Fabio Babiloni:** Resources, Supervision. **Patrizia Mancini:** Resources, Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare no conflict of interest.

Data availability

Data will be made available on request.

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