Neurocognitive factors in sensory restoration of early deafness: a connectome model

Andrej Kral, William G Kronenberger, David B Pisoni, Gerard M O'Donoghue

Progress in biomedical technology (cochlear, vestibular, and retinal implants) has led to remarkable success in neurosensory restoration, particularly in the auditory system. However, outcomes vary considerably, even after accounting for comorbidity—for example, after cochlear implantation, some deaf children develop spoken language skills approaching those of their hearing peers, whereas other children fail to do so. Here, we review evidence that auditory deprivation has widespread effects on brain development, affecting the capacity to process information beyond the auditory system. After sensory loss and deafness, the brain's effective connectivity is altered within the auditory system, between sensory systems, and between the auditory system and centres serving higher order neurocognitive functions. As a result, congenital sensory loss could be thought of as a connectome disease, with interindividual variability in the brain's adaptation to sensory loss underpinning much of the observed variation in outcome of cochlear implantation. Different executive functions, sequential processing, and concept formation are at particular risk in deaf children. A battery of clinical tests can allow early identification of neurocognitive risk factors. Intervention strategies that address these impairments with a personalised approach, taking interindividual variations into account, will further improve outcomes.

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Introduction

Sensory systems enable us to engage with the environment. Reception of sensory information depends on the integrity of specialised receptor cells that encode physical stimuli and transduce them for the brain's information-processing machinery. Loss of neurosensory input affects quality of life profoundly and is a major contributor to the global burden of disease through years lived with disability.[1] The prevalence of sensory impairment increases exponentially with age. WHO estimates that 360 million individuals globally have disabling hearing loss, which is the fifth most important cause of years lived with disability.[1] Advances in biomedical technology have led to the development of effective prosthetic devices that partly restore sensory function, even when sensory cells are lost completely. Cochlear implants, which are used to treat severe to profound sensorineural hearing loss, have become the most successful neuroprosthetic device, with more than 350 000 recipients worldwide.[2] Retinal and vestibular implants have also been developed and, although showing considerable promise,[3,4] their clinical success has not yet reached the level of cochlear implants. Sensory impairments not only frequently accompany other neurological diseases but also result in neurocognitive impairments. Because of the efficacy of cochlear implants, the auditory system has become a model in which to investigate sensory loss, sensory restoration, and related neurocognitive outcomes. This Review, therefore, focuses on neurosensory restoration in deaf children.

Restoration of components of the sensory experience with neuroprosthetic devices, although degraded relative to normal sensory functioning, allows for development of proximal cognitive skills dependent on that experience—eg, most deaf children who receive a cochlear implant at an early stage develop spoken language skills.[5] Less frequently considered, however, are the downstream, distal, cognitive effects that are not related directly to sensory loss—eg, effects on working memory and attention. The brain is a dynamic self-organising system that develops based on reciprocal experiences between neural activity and stimulation from the environment.[6,7] Auditory experience provides temporal patterns to the developing brain,[8] which could be important for developing sequential processing abilities such as pattern detection, sequential memory, and sustained attention in general.[9,10] As a result, limitations in auditory experience during development might affect neurocognitive functioning well beyond spoken language. Therefore, sensory disorders—particularly those emerging in childhood—can have detrimental neurocognitive outcomes that are of great interest to neurologists. Conversely, restoration of sensory functioning with neuroprosthetic devices such as cochlear implants can reverse or reorganise some neurological and neurocognitive effects of sensory loss.[11]

The aim of this Review is to demonstrate the implications of a connectome model for understanding variability in outcomes after sensory loss and later neurosensory restoration, using cochlear implantation in congenitally deaf children as a framework. We aim to show how this framework has important implications for the clinical assessment and treatment of individuals with sensory impairment and can serve as a model for differentiation of proximal and distal effects of hearing loss from other sources of outcome variability. As the prevalence and effectiveness of neurosensory prostheses increases, such a framework will be relevant for both clinical practice and research.

Application of a connectome model to neurosensory restoration

The connectome is a network map of effective synaptic connections and neural projections that comprise a

nervous system[12] and shape its global communication and integrative functions. Because brain development is a self-organising process, development of the connectome is highly dependent on sensory experience. As a result, sensory loss can be thought of as a connectome disease—ie, an abnormal bias in the individual wiring and coupling pattern of the brain that has implications for adaptation to a neuroprosthetic device as well as downstream neurocognitive effects. Such bias might result in stronger coupling to the remaining sensory systems, reorganisation within the affected sensory system, or a different use of the system with respect to its interactions with other sensory systems,[13–16] motor control,[17] or attention.[6] This process accounts for the abnormal visual dominance in perception after congenital deafness.[18,19] Furthermore, higher order neurocognitive functions and other sensory systems can access the auditory cortex via top-down interactions—eg, for scaling and calibrating other sensory systems for temporal information processing.[6,20] Such access could be compromised by early deafness.[6,21] Application of a connectome model to individuals with sensory impairment suggests that outcomes of hearing loss and subsequent cochlear implantation will extend beyond the direct result of sensory loss—eg, perception of spoken language in the case of hearing. As a result, factors accounting for individual differences and variation in clinical outcomes after cochlear implantation will not be confined to the auditory system itself—they might range from effects at the cellular level to those at the social level and reveal themselves in complex cognitive functions.

Neurosensory restoration with cochlear implants

Sensory neuroprosthetic devices mimic the natural physiology of sensory organs by electrical stimulation of neurons that normally innervate receptor cells. When placement of a sensory neuroprosthetic device is successful, this electrical stimulation can be interpreted by the brain as sensory input. In neurosensory disorders, the first order neurons of sensory systems frequently survive in sufficient numbers and can be stimulated artificially with neuroprosthetic devices.[22] Cochlear implants (figure 1) accomplish this stimulation with an external device (consisting of a microphone, speech processor, and transmitter coil) and an internal device (which is implanted behind the ear and includes receiver electronics and an electrode array). Sound is collected via the microphone and is sent to the speech processor worn behind the ear; the processor converts the speech sounds into electrical impulses and transmits them through intact skin from the transmitter coil to the receiver electronics. The receiver–stimulator package is placed subcutaneously and is fixed on the mastoid bone; this package receives electromagnetic signals and delivers them through lead wires to an electrode array placed in the cochlea. The electrode contacts can exploit the tonotopic arrangement of nerve fibres, with high sound frequencies represented at the cochlear base and low frequencies at the apex. Activation of the implant generates an electrical response in selective auditory nerve fibres, which is carried to the auditory cortex and is interpreted as an auditory input.

Cochlear implants carry 12–22 stimulation contacts distributed longitudinally along the electrode array. With this arrangement, the tonotopic organisation of the auditory nerve can be exploited by activation of different electrodes depending on their sound spectrum. By applying a sequence of current pulses, the temporal coding of the ear can be mimicked.[2] The temporal code is translated very accurately into auditory nerve fibre

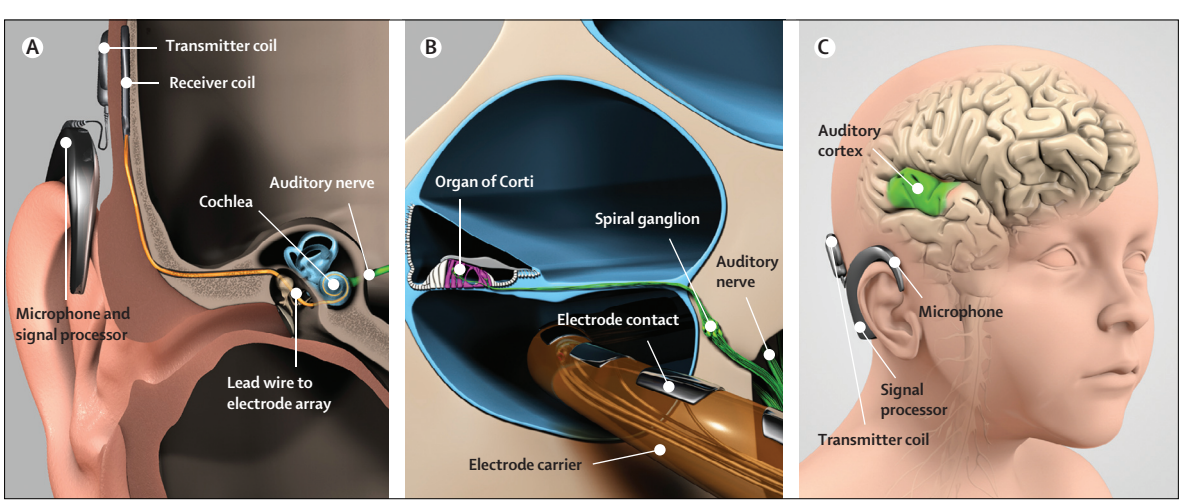

Figure 1: **Neurosensory restoration with prosthetic devices**
Cochlear implants consist of internal (A, B) and external (A, C) components. The spiral ganglion and fibres of the auditory nerve (green, B) are the targets for stimulation, bypassing the non-functional organ of Corti (red, B). Activation of the implant generates an electrical response in selective auditory nerve fibres (B), which is carried to the auditory cortex (green, C) and interpreted as an auditory percept. The auditory cortex (C) is shown on the same side as the implant for illustrative purposes, but in reality the projection is mainly contralateral.

responses,[23,24] whereas spatial coding lags behind that of the normal ear,[24] causing cross-channel interference and an absence of detailed spectral information. Furthermore, the range of intensities that electric hearing can represent is limited.[24] However, because of the robustness of speech perception, even under degraded conditions,[25] speech recognition and perception is still possible with cochlear implants. With modern multi-channel stimulation techniques, performance exceeding 90% of sentence recognition in quiet settings is possible for some recipients.[26,27] Testing without context (eg, monosyllabic tests) can cut performance from more than 90% to 55–60%,[26] showing that recipients of cochlear implants rely heavily on extensive post-processing in the brain. Such enhanced auditory receptive abilities by relying on context can be gained at the cost of increased listening effort,[28–30] which if considerable might risk depleting the cognitive reserve available for other cortical processing requirements. Thus, central processing of sensory information, particularly if it is an impoverished representation of normal input, is key to the clinical success of neural prostheses.

Brain development and sensory loss

Sensory loss and restoration in children occur in the context of a dynamic developing brain. Brain development includes a sequence of events, from gene transcription through to neurogenesis (and neuronal death), neuronal migration, development of neuron-to-neuron contacts (and their elimination), and formation of central pathways, with the aim of eventually generating a functional brain connectome (figure 2). The juvenile brain adapts rapidly to the environment and is, therefore, highly sensitive to loss of sensory input.[6,7,31] Development of the afferent auditory pathway starts before cochlear function is established and continues afterwards.[32] Since the human cochlea is functional from weeks 24–26 after conception, some processes affected by the environment might start in utero. Even before the onset of auditory function, loss of cochlear cells might result in death of subsequent auditory neurons in the brainstem.[33,34] Therefore, the age at onset of cochlear deficits in utero might affect profoundly the functional integrity of auditory pathways and, as a result, higher order brain systems and functions that rely on this sensory input.

Cortical development accelerates after birth.[11,35] Shaping of cortical circuits—synaptogenesis and synaptic elimination (pruning)—takes place in human beings from shortly before birth until adolescence (figure 2A). Maturation of myelin sheaths extends into adulthood.[36] Synaptic counts in the human cortex, a reflection of the brain's computational power, peak between the first and fourth year of life,[37] probably to facilitate development that is attuned by experience (experience-expecting development)—eg, spoken language acquisition.[35,38] Our innate genetic programme, therefore, includes periods of high susceptibility to environmental modification (sensitive periods), with augmented plasticity of neuronal connections at young ages.[39,40] Hearing deprivation during early development prevents functional maturation, delays cortical synaptogenesis, and increases subsequent synaptic elimination,[11,41] ultimately affecting central functions such as intensity coding, cortical

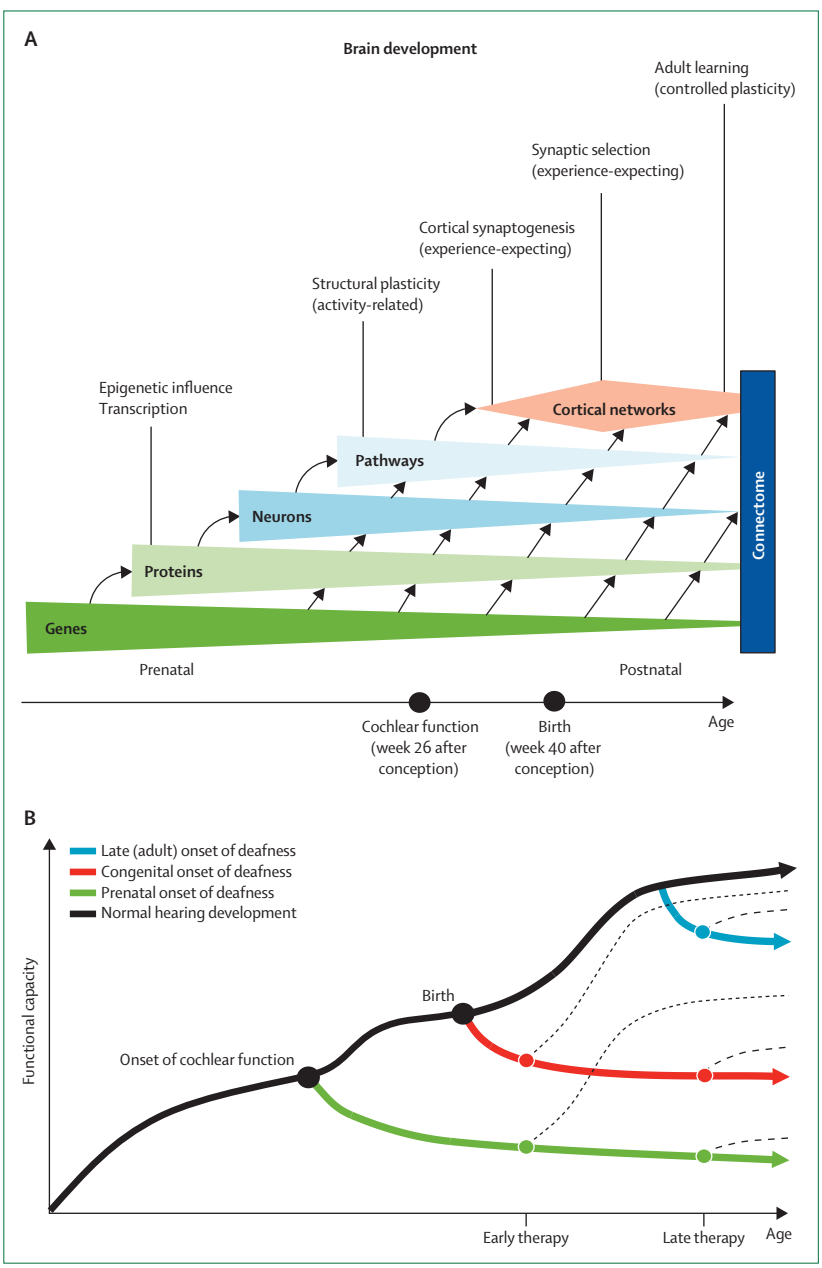

Figure 2: **Developmental events generating the brain's connectome and auditory function**
(A) Simplified sequence of selected human developmental processes depending on function and sensory input relative to onset of hearing and birth. (B) Schematic showing that functionality of the auditory system increases during development. Prenatal deafness (green) has the greatest effect on potential functionality. Congenital deafness (red) prevents many maturational steps. Early therapy (dotted lines) within the sensitive period can exploit juvenile plasticity and allows for large improvements in function. Late therapy (dashed lines) shows sufficient outcomes only with late onset of deafness (blue).

column functioning, cochleotopic representation, representation of auditory space, and corticocortical interactions including top-down control and auditory object formation.[6] Effective stimulation through a cochlear implant during a sensitive period in early development can exploit juvenile plasticity, induce maturation, and compensate for these deficits in animals and children.[11,41,42]

The residual functional capacity of the auditory system is determined by the age at onset of deafness, which restricts and modifies further maturation, and the extent of degenerative changes that happened after onset of deafness (figure 2B). However, the extent of neurodevelopmental central auditory deficits diminishes as the age at onset of deafness increases—ie, from the prenatal period to congenital, early developmental, and late developmental stages. Another factor influencing neurodevelopmental outcomes is brain plasticity at the age of intervention: early intervention within a sensitive period prevents further degenerative changes, induces functional maturation of the brain, and results in better outcomes than does late intervention (figure 2B). Late intervention leads to insufficient adaptation and, thus, poor outcomes irrespective of whether onset of deafness was prenatal or congenital; late intervention provides meaningful results only if the auditory system matured with previous acoustic hearing (also pertains to acquired and progressive hearing loss). As a result, diagnosis and treatment of hearing disorders as early as possible has become routine clinical practice,[5,41,43] with implementation of national neonatal hearing screening programmes in many countries.

	Cause or mechanism	Effect on the auditory system
Peripheral effect		
Loss of hair cells	Genetic or environmental; environmental noise, potentially excitotoxic to auditory nerve fibres	Loss of transduction of acoustic inputs; unable to combine electrical and acoustical hearing
Loss of supporting cells	Genetic or environmental	Fewer surviving spiral ganglion cells, less potential for regeneration therapy
Depleted spiral ganglion cell population	Dependent on age at onset (earlier onset, greater effect); loss of trophic factors from supporting cells; loss of trophic factors from hair cells; neurotoxicity from overstimulation	Higher threshold, poorer channel separation, smaller dynamic range
Pattern of degeneration (cochlear dead regions)	Genetic	Cochlear regions of non-responsiveness
Changes in synapses and neurons (synaptopathy and neuropathy)	Genetic	Despite presence of hair cells, evoked neuronal activity unreliable; auditory performance degraded
Central effect		
Neuronal and synaptic degeneration	Dependent on age at onset, duration, severity of deafferentation	Early hearing loss can lead to loss of central neurons and degenerative functional and morphological changes in synapses
Plastic reorganisation after hearing loss	Plasticity depends on age at onset; extent depends on severity of sensory loss, rate of progression of sensory loss, and duration of sensory loss	Neural resources for electrically stimulated cochlear regions might be overtaken by those serving regions with residual hearing; related to the extent of reorganisation
Cross-modal reorganisation	Plasticity depends on age at onset; severity and duration of sensory loss; strategy of sensory adaptation	Neuronal resources diverted to visual or somatosensory processing, potentially affecting performance after hearing restoration
Binaural hearing	Asymmetric hearing thresholds between ears	Reduced localisation ability compromising hearing in complex environments
Additional central deficits	Genetic and environmental	Hearing restoration will be compromised by associated cognitive difficulties
Neurocognitive effect		
Executive function	Auditory deprivation and language delays	Language, comprehension, learning, and social–behavioural deficits
Sequential processing	Auditory deprivation	Deficits in sequence processing and planning
Concept formation	Auditory deprivation and language delays	Reduced conceptual learning, difficulties in problem solving
Visual processing	Compensation of the absence of hearing	Redistribution of attention to the periphery; reduced sequence learning
Device-related effect		
Electrode size and form	Engineering design of the electrode array	Some designs facilitate more independent channels, others decrease cochlear trauma; advanced imaging allows customisation of electrode arrays to cochlear microanatomy
Speech coding strategy	Engineering design of the speech processor	More independent stimulation channels, higher rates of stimulation, current steering, etc, to enhance representation of speech signals
Electroneural interface	Biofunctional electrode array	Neurotrophic factors released by the implant attract primary neurons closer to the electrodes, reducing stimulation currents needed
Position of the device relative to neurons	Implantation procedure and electrode array selection; engineering design of the electrode array	Closer apposition of electrode to the neurons, less fibrous tissue reduces current spread and lowers impedance and energy requirements of the system
Tissue damage due to implantation	Implantation trauma; penetration into the scala vestibuli (vestibular duct) or damage to the basilar membrane and spiral ligament	Leads to inflammatory response with loss of neurons, sometimes in patches, causing so-called holes in electric hearing

In addition to these factors, social factors are known to play a major part in language development.

Table 1: **Known and supposed factors contributing to interindividual variation among deaf children**

Variability in clinical outcomes after cochlear implantation

Early cochlear implantation compensates for most deficits caused by profound hearing loss in childhood.[41] Deaf children who receive a cochlear implant early in life and have normal cognitive capacity show language learning trajectories similar to their hearing peers.[5] One of the hallmarks of cochlear implant outcomes, however, is the enormous variability reported in auditory, speech, and language functioning after implantation.[5,27,44–46] Loss of hearing has cascading neurological and neurocognitive effects: because no part of the brain works in isolation, loss of a sensory system such as hearing also affects other functions, including higher order neurocognitive tasks.[47] In addition to making important contributions to outcome variability (table 1), factors ranging from central neural characteristics (including effects on brainstem, midbrain, and the thalamocortical auditory centres) to social experiences and parental interaction can have substantial effects on both proximal and distal cognitive outcomes after implantation.

Neuronal plasticity as a correlate of learning incorporates molecular changes in neurons and synapses and, as a result, on connectome adaptations. The major histocompatibility system has a function in synaptic development and plasticity.[48,49] In view of the high variability of this system, it is not surprising that the capacity for learning can differ substantially between individuals. Work in animals shows both variability and constancy of specific corticocortical and subcortical connections under conditions of auditory deprivation (figure 3).[15] Tracing anatomical connections shows a complex pattern of feedback projections from other areas into the feline primary auditory field A1. In congenitally deaf cats, some connections are stronger, some weaker, and some connections have no counterpart in hearing animals (ectopic connections).[15] The auditory subcomponent of the connectome in human beings (figure 4) incorporates the substrate for implicit memory (in connection with basal ganglia and cerebellum) and contributes to explicit declarative memory and spatial orientation (in connection with the entorhinal cortex and hippocampus), fear memory (in connection with amygdala), and attention.[50,51] Variability in development of these neural circuits in response to auditory deprivation and restoration will probably affect higher order neurocognitive and psychosocial outcomes after cochlear implantation.

Individuals with normal hearing use various listening strategies—eg, for tone-in-noise detection[52] or pitch perception[53]—for which multiple acoustic cues might provide the same information. Sensory loss and auditory prostheses could degrade the specific cues needed by some people, and these individuals will struggle after implantation of a cochlear implant to a greater extent than will people who use cues that are reliably preserved. For example, the language circuit includes a dorsal and a ventral processing route;[54] individuals preferentially activating the ventral (non-phonological) route usually become poor performers in speech understanding after cochlear implantation.[55,56] Modern imaging techniques are a promising approach for objective detection of individual adaptations.[56,57]

The social environment is another key factor for neurocognitive development.[58] Parental sensitivity and cognitive stimulation affect language outcomes in children with a cochlear implant as strongly as does age at implantation,[59] and characteristics of the family

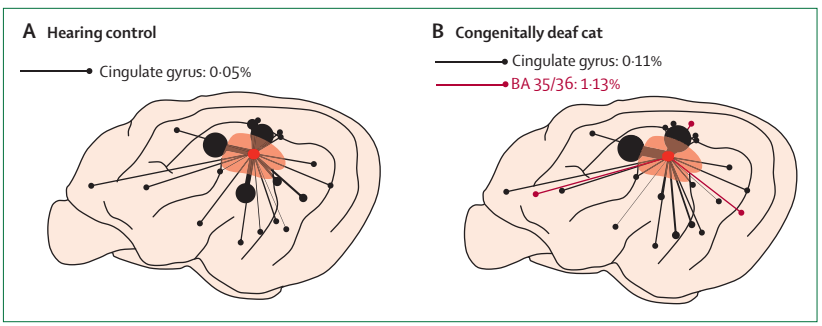

Figure 3: **Auditory component of the brain's connectome in cats**
Data taken from ref 15. Illustration of cortical anatomical connections in hearing cats (A) and congenitally deaf cats (B). The red dot (primary auditory field) depicts the area of placement of the dye to stain the connections. The strength of connections (black lines) is proportional to the line thickness. Ectopic connections (not found in hearing controls) are shown by red lines. The percentages represent the proportion compared with all connections of the given area. BA=Brodmann area.

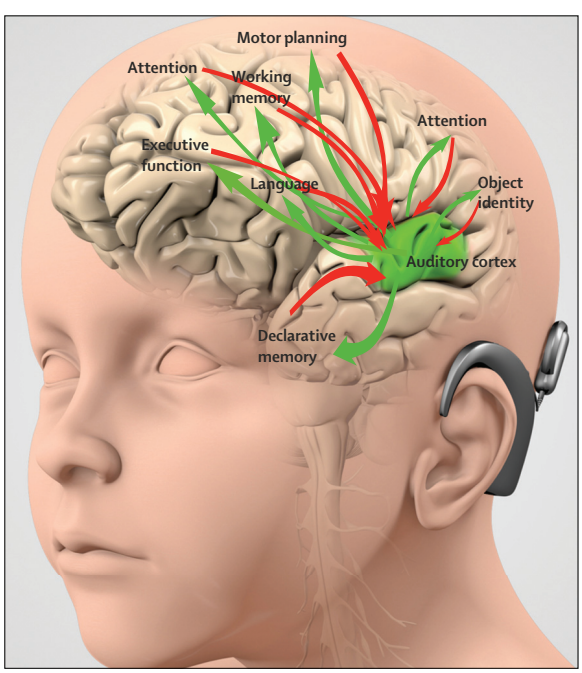

Figure 4: **Auditory component of the human brain's connectome**
Illustration of interactions of the human auditory cortex with higher order areas involved in cognitive functions. Locations of the functions on the brain are schematic. Bottom-up connections are shown in green, top-down in red. The thickness of the lines does not reflect connection strength. The speech processor and the active cortex are shown on the same side of the brain for illustration purposes.

environment influence executive functioning outcomes after implantation.[58] Social interactions provide early experiences of language, including vocabulary, verbal comprehension and reasoning, and verbal concept formation. These experiences, in turn, become the building blocks for language skills that support the later development of speech perception—eg, using context and reasoning to facilitate speech perception. Language development is an important building block for downstream neurocognitive development.[60–62]

There is a dynamic, reciprocal interplay of language, sensory experiences, and neurocognitive outcomes during development, with each supporting the others to produce holistic functional and behavioural outcomes in people with a cochlear implant. For example, better sensory functioning from the cochlear implant is related to stronger and more robust language skills;[63] stronger language skills predict better neurocognitive outcomes; and neurocognitive functioning acts to support language.[64,65] The complex interdependence of different brain subsystems, with different developmental timelines, results in the striking interindividual variability in neurocognitive outcomes after neurosensory restoration.

See Online for appendix

Clinical assessment of neurocognitive outcomes

For prelingually deaf people (ie, individuals born deaf or who lost their hearing before the acquisition of spoken language) who received a cochlear implant at an early stage, at least three related areas of neurocognitive functioning are at risk for delayed or atypical development:[9,64,66] executive functioning; sequential processing and sequence learning; and concept formation. Development of these neurocognitive domains is highly dependent on auditory experience and spoken language skills, both of which are delayed substantially at some point in all people with a cochlear implant as a result of early deafness.[47] Examples of appropriate tests for clinical assessment of neurocognitive domains are listed in table 2 and the appendix.

Executive functioning

Executive functioning is defined as the cognitive control and oversight processes needed to undertake planned goal-

	Explanation	Age range			Assessment	
		Preschool (3–5 years)	School age and adolescent (6–17 years)	Adult (≥18 years)	Below average	Problematic
Fluid intelligence (non-verbal IQ)	Reasoning and novel problem-solving that does not rely on language or fund of knowledge	DAS-II picture similarities subtest	WISC-V matrix reasoning subtest	WAIS-IV matrix reasoning subtest	T<40; scaled <7	T<30; scaled <4
Executive functioning (short-term and verbal working memory)	Holding sequence of verbal stimuli in memory while engaging in another cognitive activity; immediate memory for language-based stimuli	Leiter-R forward memory test (uses pictorial stimuli that are easily verbally encoded by the child)	WISC-V digit span and letter–number sequencing subtests	WAIS-IV digit span and letter–number sequencing subtests	Scaled <7	Scaled <4
Executive functioning (inhibition–concentration)	Effortful delay of action in the service of assessing and responding appropriately to stimuli	Conners K-CPT-2	TOVA	TOVA	T>60; standard <85	T>70; standard <70
Executive functioning (controlled cognitive fluency)	Sustained, efficient concentration skill under time pressure—eg, crossing out all pictures of animals from a complex array within a time limit	Leiter-R attention sustained subtest	WISC-V coding subtest	WAIS-IV coding subtest	Scaled <7	Scaled <4
Category-based visual concept formation	Categorisation of ideas and stimuli based on sensory or functional features	WJ-IV concept formation subtest	WJ-IV concept formation subtest	WJ-IV concept formation subtest	Standard <85	Standard <70
Spoken language concept formation	Comprehension of linguistic ideas	DAS-II verbal comprehension subtest	NEPSY-II comprehension of instructions subtest	WJ-IV understanding directions subtest	T <40; scaled <7; standard <85	T<30; scaled <4; standard <70
Executive functioning behaviour checklist	Questions (to caregivers or patients) with answers using quantitative scales	LEAF (preschool version)	LEAF	LEAF (adult self-report version)	Score >4	Score >9

T scores are norm-based scores with a mean of 50 (SD 10); scaled scores are norm-based scores with a mean of 10 (SD 3); standard scores are norm-based scores with a mean of 100 (SD 15).Conners K-CPT-2=Conners' Kiddie Continuous Performance Test, 2nd edn. DAS-II=Differential Ability Scales, 2nd edn. LEAF=Learning, Executive, and Attention Functioning Scale. Leiter-R=Leiter International Performance Scale-Revised. NEPSY-II=a developmental NEuroPSYchological assessment, second edition. TOVA=Test of Variables of Attention. WAIS-IV=Wechsler Adult Intelligence Scale, 4th edn. WISC-V=Wechsler Intelligence Scale for Children, 5th edn. WJ-IV=Woodcock-Johnson IV.

Table 2: **Suggested testing repertoire for diagnosis of cognitive deficits in children with congenital hearing loss and cochlear implants before and after implantation**

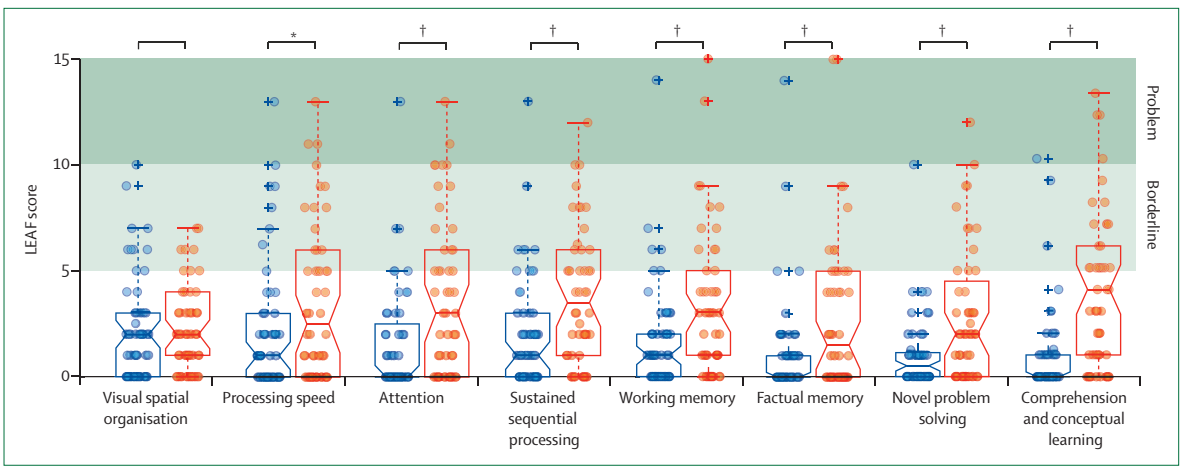

Figure 5: **Whisker plot of LEAF questionnaire findings in children with early cochlear implant and controls**
Data taken from reference 47. Children with cochlear implants are shown in red and age-matched controls with normal hearing in blue. Individual datapoints are depicted as circles; dotted vertical lines show the range of the data (not including outliers beyond 99·3% of the whole population); the box depicts the IQR; the horizontal intersection line signifies the median; statistical outliers are marked by a cross. LEAF scores are raw scores based on sums of items as rated by parents. Scores range from 0 to 15 and are criteria-referenced, with 0–4 denoting no significant problem, 5–9 denoting a mild or borderline problem, and ≥10 denoting a problem in the area assessed by the LEAF subscale. LEAF=Learning, Executive, and Attention Functioning Scale. *Difference between controls and children with cochlear implant, p<0·05. †Difference between controls and children with cochlear implant, p<0·001.

directed activities.[67] Executive functioning consists of multiple components—ie, working memory, controlled attention, self-monitoring, organisation, inhibition, flexibility-shifting, and goal direction.[68] Verbal working memory,[69,70] controlled cognitive fluency,[67,71] redistribution of attentional resources,[21,72,73] and inhibition–concentration are at risk for delays in individuals with early deafness despite cochlear implantation.[66,74,75] Verbal working memory is assessed with neurocognitive methods that require individuals to hold a sequence of familiar verbal stimuli—eg, digits, letters, or words—in immediate memory while simultaneously engaging in another cognitive activity, such as reversing the order of test items or completing a simple mental calculation (appendix).[76] Inhibition–concentration tests require a combination of controlled attention and active management of automatic responses to respond correctly to a target stimulus. Controlled cognitive fluency can be assessed with neurocognitive tests requiring rapid completion of multiple visual–perceptual or simple decision-making tasks under conditions needing sustained attention, concentration, and mental effort.[67,71] These executive functioning domains can be tested with standard behavioural methods; some, however, need software or hardware components (table 2). Although delays in processing in these three areas of executive functioning have been shown in many people with cochlear implants,[66,74,75] considerable individual differences are also present in children who receive an implant early (figure 5); therefore, an individualised approach to assessment of these at-risk areas of executive functioning is warranted.

Sequential processing

Early auditory deprivation can affect sequential processing skills at several levels.[9,77] Clinical assessment of sequential processing and sequence learning might, therefore, be warranted for people with cochlear implants. Although no tests in common use measure sequential processing alone, in isolation from other areas of neurocognitive functioning, sequential processing is a central component of several neurocognitive domains that can be assessed systematically with existing tests. For example, verbal short-term memory tests (eg, digit or letter spans) that assess sequential processing and memory of linguistic stimuli showed developmental delays in many people with a cochlear implant.[74,75,78] However, poor performance on verbal memory span tests can reflect either language or sequential processing deficits (or both). On the other hand, spatial, design, or tactile sequential processing and learning tasks are not constrained by language and allow for assessment of more domain-general non-verbal memory and sequential processing deficits. On a spatial span task, for example, individuals must reproduce a series of sequential spatial locations shown by an examiner or computer.[79] Sequence processing tasks that do not entail memory include sequential matrix reasoning tests, for which individuals select a response option that completes a sequence of several previous steps,[80] and motor sequencing tests such as fingertip tapping.[10] Although delays and disturbances in sequential processing have been reported in some people with a cochlear implant on tests of spatial memory and fingertip tapping,[9,81] this is not always the case, particularly with spatial memory tests.[74,75,78] As with executive functioning, large individual differences in sequential processing skills within the population with cochlear implants necessitate an individualised patient-centred approach to assessment.

Concept formation

Concept formation involves the categorisation and differentiation of stimuli based on sensory or functional features. Deaf children in general,[82] and those with a cochlear implant in particular,[83] are at high risk for delays in concept formation (figure 5) that are, in part, affected by language and working-memory deficits. Tests of concept formation that need only non-verbal reasoning of simple one-step analogies[80] typically do not show delays in people with a cochlear implant,[83] but concept formation tests that require individuals to hold and process several stimulus characteristics simultaneously–eg, the concept formation subtest of the Woodcock-Johnson Tests of Cognitive Abilities—show substantial delays in people with a cochlear implant.[83] Deficits in the formation of abstract relationships and concepts could create additional problems in language comprehension, which requires conceptual understanding of more complex ideas and relations. The ability to integrate and combine smaller linguistic units to produce larger, more meaningful units can be difficult for people with a cochlear implant because of the increased flow of information and amount of concept formation entailed; linguistic tasks such as following directions, answering questions, and comprehending spoken or printed language need this level of integration and connectivity. These downstream influences of concept formation on language comprehension can be assessed by tests of understanding directions and comprehension of spoken language (table 2).

Behaviour checklists

In addition to assessment with clinical performance neurocognitive tests, systematic assessment of neurocognitive functioning in real-world daily behaviour is also important. A commonly used technique is a behaviour checklist, consisting of a series of questions rated on a quantitative scale by either the person with the cochlear implant or a caregiver. Both the Behavior Rating Inventory of Executive Function (BRIEF) and the Learning, Executive, and Attention Functioning Scale (LEAF) have been used to assess executive functioning, sequential processing, and concept formation skills in people with a cochlear implant.[47] Scores on subscales from these rating checklists provide further converging diagnostic information about neurocognitive skills in daily functioning while placing little burden on the assessor. Research with BRIEF and LEAF in a sample of children who received a cochlear implant at an early stage showed that the risk of problems with executive functioning in daily behaviour was three to four times greater compared with their peers with normal hearing (figure 5).[47] This outcome was not related to age at implantation, since 80% of children were implanted before age 4 years.[47]

Other domains of neurocognitive functioning

Scores on neurocognitive at-risk areas should be interpreted in the broader context of other domains of neurocognitive functioning. Measures of non-verbal (fluid) intelligence and language skills, for example, might provide an explanation and better understanding of other areas of neurocognitive functioning for individuals with a cochlear implant, even though, as a group, people with a cochlear implant are not at risk for lower fluid intelligence scores.[66]

Clinical interventions to improve neurocognitive outcomes

Rapid growth in research on neurocognitive assessment of people with a cochlear implant has not yet been accompanied by parallel growth in evidence-based neurocognitive intervention options. Such progress will be important for addressing potential neurocognitive sequelae of hearing loss. Promising steps towards neurocognitive interventions for people with a cochlear implant have been made in two areas. First, executive functioning interventions have been designed for children with normal hearing that can be applied to individuals with a cochlear implant. Second, additions to conventional speech–language interventions for people with a cochlear implant can incorporate specific processing strategies for improving neurocognitive development.

Executive functioning interventions

In individuals with normal hearing, emerging evidence from randomised clinical trials indicates that some interventions can improve executive functioning.[68,84] Approaches that have shown promise for enhancing executive functions in people with normal hearing include computer-based working memory training programs,[85,86] activity-discipline programmes (eg, martial arts training),[87] school-based courses that teach executive functioning skills,[88] and parent-based or family-based methods that teach and encourage executive functioning skills.[89]

Specific examples of computer-based executive functioning training programs include Cogmed Working Memory Training (CWMT)[62,85] and N-back Working Memory Training (NBWMT).[86] These two programs present individuals with computer-based exercises similar to a video game, in which items are memorised and the difficulty increases as performance improves. In studies of CWMT and NBWMT, including a study of people with cochlear implants,[90] improvements have been seen on trained tasks and similar memory tasks (near-transfer), but far-transfer results showing change in executive functioning behaviours in daily life have been less consistent.[91]

Other approaches to executive functioning training that have shown promise in people with normal hearing include school-based training courses—eg, Tools of the Mind,[88] Promoting Alternative Thinking Strategies,[92] the Chicago School Readiness Project,[93,94] and the Thirty Million Words Project.[95] These interventions provide learning experiences for children by teaching and encouraging executive functioning and other adaptive

behaviour skills directly and by creating a positive learning and family environment that emphasises cognitive development.

Incorporating neurocognitive interventions into speech–language therapy

Because of the strong associations between language and executive functioning (particularly working memory) in people with a cochlear implant[64] and in individuals with normal hearing,[60,61] speech–language interventions can improve neurocognitive outcomes in people with a cochlear implant. Such methods are well established, effective, and important for habilitation to the device.[96] Moreover, speech–language interventions frequently incorporate practice with executive functioning skills—eg, controlled attention (to elements of the speech signal or to components of language), inhibition (focusing on one aspect of sound or language while ignoring competing stimuli), and cognitive efficiency (rapid and efficient processing of language).[97] Novel, computer-based, auditory training exercises[98] and non-word repetition training[99] (active practice with processing and identification of auditory stimuli with the aim of improving auditory or language processing skills) also include a substantial component of executive functioning in the form of controlled attention and active regulation of higher order cognitive processes. In the few studies that have investigated changes in executive functioning in people with a cochlear implant after speech–language therapy, greater improvements in speech and language skills than in executive functioning skills have been reported.[100]

Early research on the effectiveness of neurocognitive interventions for individuals with a cochlear implant has shown positive near-transfer effects, but evidence for generalisation and far-transfer effects or long-term improvement is sparse.[98,100] Ultimately, an integrated approach that incorporates executive functioning and neurocognitive interventions derived from samples of people with normal hearing into speech–language therapies offers the best promise for improving far-transfer and long-term outcomes in people with a cochlear implant.

Future directions

Sensory loss is prevalent in human populations and can have profound effects on development, adjustment, and quality of life. Neurosensory prostheses offer the potential to mitigate the effects of sensory loss, restoring some components of sensory functioning. However, sensory loss has distal effects that extend well beyond the sensory system and related brain functions, with pronounced effects on central neurological and higher order neurocognitive functioning.

Research and clinical experience with cochlear implants provides specific support for application of a connectome model to neurosensory restoration after cochlear implantation. It is important to emphasise that downstream influences on central neural and neurocognitive development probably arise as a result of sensory loss and not as a result of sensory restoration by the cochlear implant; in fact, sensory restoration in a connectome model offers the potential for improvement in outcomes. Research on brain development after deafness and cochlear implantation can serve as a model system for understanding outcomes from other domains of human sensory restoration.

Gene therapy and tissue engineering might substantially improve the fidelity of sensory restoration, mainly for diseases in which the underlying cause is monogenetic and has resulted in few degenerative changes in the sensory organ—eg, isolated synaptopathies or transduction channel mutations.[101–103] Improving the biological infrastructure of the implanted auditory system could enhance the capacity to receive and process sensory information, allowing more patient-specific stimulation strategies, and might ultimately obviate the need for cochlear implantation.[104]

One important area for future research is development of novel interventions for congenitally deaf children who have little improvement in spoken language after receiving a cochlear implant. Currently, the enormous outcome variability is only accounted for partly by conventional demographic, device, and hearing history characteristics. A crucial, pressing, clinical problem is how to assist deaf children who fail to achieve adequate spoken language functioning despite successful implantation surgery. It has been suggested that children with cochlear implants should also be taught sign language as a means of providing language experience, in the event that spoken language does not develop.[105,106] However, this proposal has been criticised for lack of sufficient research evidence.[107]

Application of a sensory connectome model to the effects of cochlear implantation provides possible neural and neurocognitive explanations for variability in spoken language outcomes extending well beyond device and audiological characteristics. Investigation of these connectome-based explanations is a fruitful area for

Search strategy and selection criteria

We searched PubMed, ISI Web of Science, and Google Scholar with the terms "cochlear implant", "cochlear implantation", "neurocognitive", "executive function", "working memory", and "attention", for reports published between January, 2011, and November, 2015. We also included reports referenced in papers retrieved by the initial search. Our main focus was on studies that pertained to prelingually deaf children who had received a cochlear implant at an early stage (not mixed samples of people with a cochlear implant and individuals with hearing loss) and that addressed domains of neurocognitive functioning—eg, executive functioning. Where relevant, we included work in other groups for comparison.

research that could lead to intervention recommendations to benefit those who have suboptimum outcomes after implantation.

Contributors

AK elaborated the neurobiological sequalae of auditory deprivation. DBP and WGK jointly considered the neurocognitive aspects of deafness and cochlear implants. GMO focused on clinical implications of these findings.

Declaration of interests

GMO and AK report non-financial support from the Cochlear Corporation, MedEl, and Advanced Bionics. DBP and WGK declare no competing interests.

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