

Scientific Evaluation

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Extract :

(...)

Auditory bone conduction

A major distinctive and unique feature of **Forbrain**® is that auditory stimuli are delivered through bone conduction instead of air conduction [...]. This is a major asset of the product as it extends the possibilities of stimulus manipulation and presentation in a unprecedented way, resulting in an incomparable new possibilities of acoustic environment enrichment (which emerges as one of the major elements inducing passive auditory plasticity; see below). (...)

It is rather well established in the scientific literature that in addition through the air canal, or air conduction, the travelling waveform of a sound can reach the inner ear, induce a travelling wave in the basilar membrane and hence stimulate the cochlea by the

same mechanisms as normal air conduction but via bone vibration (Stenfelt et al., 2003). These observations trace back to the times of Georg von Békésy, the Hungarian recipient of the Nobel Prize in Medicine in 1961 for his contributions to understanding of the cochlea function (Puria and Rosowski, 2012). Yet, much of our modern quantitative understanding of bone conduction is due to a series of studies by Tonndorf appeared in the late 60' (Puria and Rosowski, 2012), establishing a still-valid model of bone conduction. Only recently, the studies of Stenfelt in human cadavers revealed that the most significant mechanism of bone conduction is that of fluid inertia, at least for the speech frequency region, with other potential contributing mechanisms lying within the 10 dB limit (Stenfelt and Goode, 2005). Recently, it has been shown that the contributions of both air and bone conduction to the perception of self-vocalized sounds vary as a function of frequency and the specific phoneme that it is produced, with bone conduction signals being larger at frequencies below 2 kHz and for nasal vowels, and with predominance of air conduction signals for components above 2 kHz (Reinfeldt et al., 2010).

With regard to **Forbrain**® and as a critical factor to be taken into consideration, it has to be highlighted that the cochlea, its basilar membrane and the encoding of the incoming sound signal into a neural pulse can be considered as a bottleneck through which both air conducted and bone conducted sounds converge in their way through the central auditory system (Stenfelt et al., 2003; 2005). Hence, if the amplitude and phase of a particular sound are appropriately adjusted, its cochlear signal should be cancelled out. This was already anecdotally observed by von Békésy for a 0.4 kHz tone in humans, and subsequently replicated in animals and humans for frequency ranges of 0.1 to 15 kHz (Wever and Lawrence, 1954; Khanna et al., 1976). This is important because, through the dynamic filter implemented in **Forbrain**®, unforeseen and random changes in the bone conduction signal may result that may eventually cancel out, or at least modify substantially with the air conduction signal to the very same sounds (i.e., the one uttered by the user that reaches the air canal and the emitted by the bone canal after modification by the **Forbrain**® filters resulting in unexpected, rare and potentially surprising changes in the auditory signal that it is finally transduced at the cochlea and conveyed to the central auditory system.

Air conduction thresholds are routinely obtained in clinical settings to determine the actual levels of hearing, and bone conduction thresholds are also obtained to determine true cochlear function; differences between these values represent conductive forms of hearing loss caused by pathological factors impeding sound transmission to the cochlea (Lustig, 2010). On a clinical side, bone-conduction hearing aids are being developed to augment hearing in patients with sensorineural, conductive, and mixed hearing losses (Cremers et al., 2010; Puria and Rosowski, 2012).

The consequences of feeding the auditory system back via sensations delivered through bone conduction with **Forbrain**® are important, for two independent reasons. First, it has been proposed that the vocal (motor) system sends an efferent copy or corollary discharge of the sound it aims at producing, so that the encoding of the auditory input resulting from the self-produced sounds is attenuated in the auditory system (Aliu et al., 2008; see Wolpert et al., 1995; Crapse and Sommer, 2008; Scott, 2013; see below section Audio- vocal loop and delayed auditory feedback). This way, the auditory system implements a neurophysiological mechanism that allows it to recognize the self-emitted sounds, and to disregard them from further processing, leaving the processing resources for the externally generated sounds (SanMiguel et al., 2013), with the obvious adaptive and communicative advantages. (In some regard, this shows certain parallelism with the statement commented above on "leaving your ears free to perceive external sounds").

Now, and critically, if the "natural" input of the expected voice via the air canal is manipulated by providing "unnatural" (the "extra" bone conduction feedback) and therefore "unexpected" input through the bone canal, the sensory predictions triggered by the efferent copy are therefore violated, resulting in necessary adjustments to the model of the sensory expectation. This template violation by an unexpected input results necessarily in an attentional challenge, as the auditory system identifies the incoming signal as "deviant", "rare" or "unexpected", resulting in an involuntary attention switch (Escera et al., 1998). As a matter of fact, a large body of evidence has indicated that novel or unexpected auditory stimuli trigger an involuntary attention switch toward the incoming stimulus resulting in behavioral distraction of the ongoing primary task and an concomitant adjustment of brain activity in the underlying neural network (see reviews in Escera et al., 2000; Escera and Corral, 2007; see also below the section Attention

capture and orienting response). Thus, under conditions of auditory feedback through bone conduction one might expect to submit the auditory system to a regime of constant challenge through novel or unexpected stimuli, imposing a high load of attentional demands. Furthermore, in the second place, the implementation of the gating filter introduces frequency and temporal manipulations on the emitted voice so that it further deviates the incoming signal from its efferent copy, increasing even more the attentional challenge drove by **Forbrain®**.

Nevertheless, the evidence mentioned above about involuntary attention has demonstrated that the auditory system can also cope with distracters, easily reorienting attention back to task performance after a transitory attention switch (Escera et al., 2001; Schröger and Wolff, 1998; see Escera and Corral, 2007). The final outcome of all these back and forth processes of orienting and reorienting of attention during hearing the manipulated own voice via a bone conductor might be a general improvement in the attention control capabilities, allowing an easier protection against distracters and a better focused behavior. In other words, after facing **Forbrain®** feedback for the first time with the initiation of a training protocol, and for a period that needs to be specified in future studies, the brain needs to learn to cope with and to filter out these random variations in what can be regarded as a training exercise for the executive control of attention.

Auditory function, auditory discrimination and auditory plasticity

The function of the auditory system is obviously, to encode the myriad of sounds that reach our ears to give rise to the meaningful perceptual objects, allowing us to communicate through language or enjoy music. A long tradition of research has dealt with the mathematical modeling of the representation of the basic perceptual attributes of sound, such as pitch, loudness, timbre, and spatial location, and although there is no unanimity on the basic analysis of sound in the cochlea, these models allow to predict the output of the cochlea for a given particular set of inputs (Shamma and Fritz, 2014). Yet our current knowledge on how the auditory system transforms the acoustic input into meaningful objects to give rise perception is a matter of open debate.

Compared to other sensory systems, the auditory system presents a rather complex

architecture, with several synaptic subcortical stations before information reaches the cortex. These include the cochlear nuclei, the lateral lemniscus, the superior olivary complex, the inferior colliculus, and the medial geniculate body of the thalamus, which in turn projects to primary auditory cortex (Malmierca, 2003). Besides this ascending or lemniscal auditory pathway, there exist massive descending corticofugal projections from primary auditory cortex particularly to the inferior colliculus (Suga et al., 2002). The role of these projections appears to be critical in shaping ascending auditory information by tuning neural responses in subcortical stations as a function of online or long-term plasticity (Bajo et al., 2010). The amount of sensory computation that takes place in the inferior colliculus has led some authors to suggest that this auditory station can be regarded as the equivalent to primary visual cortex (King and Nelken, 2009).

While it is evident that one major principle of organization along the auditory hierarchy, at least up to primary auditory cortex, is tonotopy, so that individual neurons responding to adjacent frequencies lie in adjacent portions of the neural tissue at a given hierarchical level, much less is known about organization in higher order areas of the auditory system. Seminal studies found that neurons in isofrequency bands of the primary auditory cortex of the cat encode for spatial preference, and more recent studies suggested an orthogonal representation of representation of spectral and temporal information even in the inferior colliculus (Baumann et al., 2011). The emerging view of current research is that the neurons in hierarchically higher order areas encode for more complex sound attributes. For example, a recent study found that individual neurons in the inferior colliculus encoded for spectro-temporal features of the delivered sounds whereas neurons in the auditory thalamus and primary auditory cortex encoded for abstract characteristics of these sounds (Chechik and Nelken, 2012). In the same line go the studies that have revealed a voice specific region in the primate temporal lobe beyond primary auditory cortex (Petkov et al., 2008) that contains voice sensitive neurons (Perrodin et al., 2011). Yet, a clear picture of how sounds are encoded to give rise to high-order auditory perception is a matter of study.

Another major principle that seems to emerge in the organization of the auditory system is that of regularity encoding (Escera and Malmierca, 2014; Nelken, 2014). Indeed, neurons along different stations of the auditory pathway, including the inferior

colliculus, the medial geniculate body and the primary auditory cortex show a functional property known as stimulus specific adaptation (SSA): they stop firing after a few repetitions of the very same stimulus while trigger robust responses when the stimulus is changed. This neuronal behavior parallels, and in fact its study was fostered by, the mismatch negativity (MMN), an auditory cognitive evoked potential elicited to a rare stimulus that deviates from the preceding repetitive background (Näätänen et al., 2007). Also, correlates of deviance detection have been recently observed in other components of the auditory evoked potentials in humans, namely the middle-latency response (MLR; Escera and Malmierca, 2014). The MMN response and the theoretical models underneath have yielded a very flourishing research area on the cognitive capabilities of the human auditory system. Essentially, these studies have been paramount to our understanding on how the auditory stimuli are represented and discriminated in the auditory system. For example, by measuring the MMN it was found that the sounds of language (phonemes) are represented in the left temporal cortex (Näätänen et al., 1997), that the neural representation of the sounds underlying MMN is related to the auditory discrimination of these sounds (Amenedo and Escera, 2000), and that it can be altered in a range of clinical conditions (Näätänen et al., 2012). As the MMN is elicited when the current input does not match a neural representation of the preceding auditory regularity, its generation can be taken as an indicator of the accuracy of sound representation in the auditory cortex.

A critical factor that has emerged as very significant in regularity encoding is that of temporal predictability. Several studies have demonstrated that the auditory system is able to drive predictions not only on the stimuli that are expected to appear based on what has been heard before, and encoded as a regularity (Haenschel et al., 2005), but also on when these stimuli are likely to happen. In this regard, it has been shown that temporal predictability enhances repetition suppression (Costa-Faidella, et al., 2011), the neural correlate of regularity encoding, and propagates downstream the auditory hierarchy the prediction signal regarding the regularity (Baldweg, 2006). As temporal predictability is enhanced by presenting the stimuli at temporal intervals, that is to say, in a rhythmic manner, it has been suggested that synchronization of brain rhythms is the neurophysiological mechanism responsible for these effects (Arnal and Giraud, 2012). Hence, by measuring the entrainment of neural oscillations one can approach the

processing of rhythmic information in the human brain.

What clearly emerges as a distinctive property of the auditory system, along with the brain in general, is its ability to undergo plastic changes as a function of the experience. This is particularly true during the so-called critical periods in early development, where short periods of massive plasticity shape the largescale structure of the sensory cortices (Hensch, 2005). However, the auditory system remains plastic even in the adulthood. A large body of evidence has shown that the auditory cortex can undergo plastic changes in response to behaviorally relevant sounds (Fritz et al., 2005; Nelken, 2009), such as those that are conditioned to reward or punishment in animal experiments. In any case, what it seems to be critical for inducing these plastic changes are the behavioral importance of the stimulus. A paramount example of this property of the auditory system is seen in the brain of musicians, who show major functional and anatomical differences compared to non-musicians (Zatorre, 2013), even at the level of encoding of musical sound properties in the inferior colliculus with generalization to the encoding of speech sound features (Kraus and Chandrasekaran, 2010). Moreover, a short period of twelve months in children aged 8-10 years with no previous musical experience seems to suffice to enhance their preattentive processing of syllabic duration and voice onset time (Chobert et al., 2014).

Yet, auditory plasticity has not only been seen for active conditions, such as the ones described in the preceding paragraph but, interestingly, for passive conditions as well. Indeed, the work of Eggermont and colleagues in cats has demonstrated that passive long-term exposure to a spectrally enhanced acoustic environment causes a massive reorganization of the tonotopic map in the auditory cortex (Noreña et al., 2006; Pienkowski and Eggermont, 2012). In these studies, animals are exposed continuously for a period of 8-15 weeks to a constant noise of a particular broadband (e.g., 5-20 kHz), and the results showed that the animals suppressed neural responses to tones in the stimulated band whereas they showed enhanced representation at the edges of the noise. Although these results have a negative connotation –altered tonotopic representation--, they show that plastic auditory changes can indeed take place even in passive conditions by exposing individuals to novel and challenging acoustic environments, and may explain non-peripheral hearing deficits, including tinnitus, in individuals exposed for years to

occupational or recreational sounds (Pienkowski and Eggermont, 2012).

A more positive note of brain plasticity induced by passive music listening (one hour daily during two months, of self-selected materials) was observed in a study of patients recovering from stroke (Särkämö et al., 2008). Patients in the music group, compared to those in a group that were presented with audio-books (same regime) or not listening at all, showed enhanced recovery in verbal memory, focused attention and several mood measurements, that remained present even after 6 months of the treatment (Särkämö et al., 2008). Similar results were obtained in subsequent studies with different clinical populations (Soto et al., 2009; Tsai et al., 2013). Yet these results need to be interpreted with caution as several mechanisms can account for the observed effects, as for example the fact that the music was pleasant, since it was self-selected by the participants, and may therefore activate the limbic system enhancing motivation and arousal (Zhang et al., 2012).

(...)

Audio-vocal loop and delayed auditory feedback

Beyond the seminal distinction between the expressive brain for language, located in Broca's area in the frontal lobe of the left hemisphere, and its comprehensive counterpart, located in the Wernicke's area in the posterior bank of the superior temporal lobe, there is plenty of everyday experience and experimental data showing that both speech perception and speech production are two mutually interdependent processes. It just takes a bad telephone connection, in which one's own voice is echoed in the earpiece with a slight delay, to realize that the auditory input affects speech production. This incidental observation was then experimentally investigated as the effect of delayed auditory feedback on speech production (Fairbanks, 1955; Yates, 1963), and subsequently proposed to one possible treatment for speech articulation problems, such as in developmental stuttering (Neelley, 1961; Lincoln et al., 2010; Unger et al., 2012). Also, speakers in different speech contexts can easily, and unintentionally pick different speaking accents, in the so-called gestural drift (Sancier and Fowler, 1997), and the most compelling observation is simply that the acoustic environment of a prelingual child determines the speech patterns s/he acquires.

From the side of the motor influences on speech perception several observations and theoretical accounts have suggested a causal role of the motor speech system, i.e., the vocal tract, on the way the sounds of language are perceived. For example, an indirect manifestation of these influences can be observed in the McGurk effect, where an illusory speech percept results from integration of incongruent auditory and visual speech cues even in very young infants (Kushnerenko et al., 2008), although its supportive value to a motor theory of speech perception has been discussed (Matchin et al., 2014). Besides, the discovery of the mirror neurons in the macaque brain and homologous regions in the human brain has led to the proposal of speech perception theories that postulate the involvement of the motor system not only regarding the vocal tract but also its whole extension in a very fine-grained manner (Pulvermüller and Fadiga, 2010). However, in spite of the plenty of evidence suggesting that the motor and the auditory systems interact with each other in producing and perceiving speech, the available evidence does not support either a model in which the motor system is a necessary component for speech perception, or that direct sensory auditory feedback is necessary for speech production (Hickok et al., 2011).

A series of functional neuroimaging studies have identified a particular auditory-related area located in the posterior part of the planum temporale of the left hemisphere that is also involved in speech production, the so-called Spt area (Hickok et al., 2000, 2003). It has been observed that Spt is activated during passive perception of speech and during covert (subvocal) speech articulation (Buschbaum et al., 2001, 2005), but appears not to be speech specific as its sensorimotor responses can be equally triggered to tonal melodies as sensory stimulation and humming as the motor behavioral counterpart (Hickok et al., 2003). Activity in this area is highly correlated with that in the pars opercularis (Buschbaum et al., 2005) --an anatomical region subserving part of Broca's area--, with which it is densely interconnected through white matter tracts (Hickok et al., 2011). Hence, by being situated in the middle of a network of auditory (superior temporal sulcus) and motor (pars opercularis) areas, the Spt has been considered as the hub of sensorimotor integration for speech and related vocal-tract functions (Hickok et al., 2010), being implicated in auditory feedback control of speech production. For example, a recent functional neuroimaging study found this region was activated by shifted, compared to non-shifted, speech feedback (Tourville et al., 2008). Also, this

area is typically damaged in conduction aphasia (Baldo et al., 2008), where patients have decreased sensitivity to delayed auditory feedback (Boller and Marcie, 1978), and in persistent developmental stutterers (Foundas et al., 2004), who benefit from delayed auditory feedback therapy (Neelley, 1961; Lincoln et al., 2010; Unger et al., 2012).

From a theoretical point of view, a state feedback control model has been put forward (Hickok et al., 2011), in which the Spt region seems to play a critical role. In this model, online articulatory control is based on feedback, but not on direct sensory feedback. Instead, online feedback control comes from an internally maintained representation of an estimate of the current dynamical state of the vocal tract. In this way feedback control is achieved primarily via internal forward model predictions whereas actual sensory feedback is used to train and update the internal model (Hickok et al., 2010). This is very relevant in the context of **Forbrain**® because, as discussed above, the sensory feedback provided by the bone conductor and the dynamic filters do really violate the internal predictions, leading necessarily to online readjustments and retuning of the internal model. According to the theoretical formulation, when a motor command is issued to the vocal tract, a corollary discharge is also sent to the internal model of the vocal tract, which represents an estimate of its dynamical state given the recent history of the system and the incoming (corollary) motor order. This state estimate is then transformed into a forward prediction of the acoustic consequences of the motor command (the sound one expects to hear). In turn, this auditory forward prediction has two consequences: 1) provides rapid internal monitoring to yield the necessary corrective feedback, and 2) compares the actual sensory consequences (the sound produced) and uses prediction error signals to update the internal model (Hickok et al., 2010).

The transparent readout of all the technicalities described above is that speech production involves not only the activation of motor speech representations but also internal representations of the sensory speech targets one aims to produce. As a matter of fact, a study conducted in my laboratory showed that persistent developmental stutterers display a deficient representation of the sounds of their native language (phonemes), in the present of preserved acoustic features representation, as measured in passive conditions (Corbera et al., 2005). Moreover, these deficient phoneme

representations correlated with the severity of the stuttering, supporting the theoretical model described above. An important implication of the model, in general and in particular regarding **Forbrain**®, is that using one's own voice is sufficient to generate corrective signals for motor speech acts, as hearing other speakers' voices is sufficient to learn and tune new motor speech patterns. Hence, one can expect that motor-speech networks in the frontal cortex are activated during passive speech listening, at the same time that a profound system recalibration is taken place online at a very subtle level during normal speech production. Now, if the expected incoming signals from the one's own voice are profoundly violated, as it occurs with **Forbrain**®, dramatic plastic changes are to be expected in the audio-vocal loop.

Of special interest in this chapter is a relatively recent study that tested the short- and mid-term effects of a treatment of adults suffering from stuttering with delayed auditory feedback using bone conduction stimulation (Stidham et al., 2006). A prototype of an antistuttering device was developed by Cochlear Ltd. (formerly Entific Medical Systems in Sweden) with the properties of a compact Baha® device (Cochlear Ltd.) adjustable to temporal cue delays of 5 to 120 ms. During the treatment, participants wore the device daily for four hours during a period of four weeks (112 hours in total). Immediately after the training, there was a significant improvement in the patients severity of stuttering behaviors as evaluated with the Stuttering Severity Instrument for Children and Adults - Third Edition (SSI3), yet these effects vanished out after six weeks post-treatment (Stidham et al., 2006). However, caution has to be taken in the interpretation of this study, as only nine patients completed the protocol, and a randomized control group (i.e., receiving no treatment) was lacking. In any case, this is suggestive of one potential uses of **Forbrain**®, as outlined below in the section relevant areas of research.

Speech in noise

While auditory and speech perception comes as natural function for most of persons, even when carried out in normal environments which are usually filled with various types of background noise, such as in busy city streets, cafeterias, concurred social events and even at the classroom, the auditory system has to implement what is known as successful speech-in-noise perception. Children, especially those with learning

disabilities, and older adults are particularly vulnerable to the effects of noise on speech perception (Bradlow et al., 2003; Ziegler et al., 2005; Kim et al., 2006). These difficulties may arise even in the presence of a normal hearing audiometry, suggesting that the underlying deficits arise from central auditory deficient mechanisms (Anderson and Kraus, 2010). Consequently, it has been proposed that some learning disabilities in children may result in part from a noise exclusion deficit, which would manifest in the presence of noise but not in quiet situations (Sperling et al., 2005; Ziegler et al., 2009). For example, Ahissar et al. (2006) found that the performance of children with dyslexia making comparative sound discriminations while listening in background noise was deficient when they were made available a short set (10) of pseudoword items, whereas these deficiencies disappeared when the set was longer (40 items). These authors argued that the auditory system extracts regularities from the ongoing stimulation, as discussed above, to form a perceptual anchor, a type of memory trace of the incoming information that links perception with memory, and that the deficit they observed in dyslexics was due to their inability to profit from extracting regularities from the ongoing stimulation due to noisy system (Ahissar et al., 2006). In older adults, on the other hand, difficulties in speech-in-noise perception have been attributed to age-related factors affecting neural synchrony (Tremblay et al., 2003; Caspary et al., 2005).

Speech-in-noise perception is a complex task involving the interplay between sensory and cognitive processes. In order to identify the target sound from or the speaker from the background noise, the auditory systems first needs to form an auditory object of what is hearing based on spectrotemporal cues. For example, the speaker's voice is identified by auditory grouping of the critical acoustic features, such as the fundamental frequency (F_0) and the second harmonic of the stimulus (H_2) defining the vocal pitch (Anderson and Kraus, 2010). Yet, these features of the speech signal are clearly different from the competing noisy background and, as demonstrated by several studies, are clearly extracted and encoded at the level of the auditory brainstem (Anderson et al., 2010). For example, several studies have demonstrated that the auditory brainstem response recorded from the human scalp known as the Frequency Following Response (FFR; Skoe and Kraus, 2010; Chandrasekaran and Kraus, 2009; see Figure 1) is delayed and attenuated when obtained to stimuli presented in background noise conditions (Cunningham et al., 2001; Anderson and Kraus, 2010). Moreover, several recent studies

have shown that different training programs can help improving speech-in-noise perception by mechanisms of enhancing the encoding of the speech relevant features in the auditory brainstem (Anderson and Kraus, 2011; Kraus, 2012).

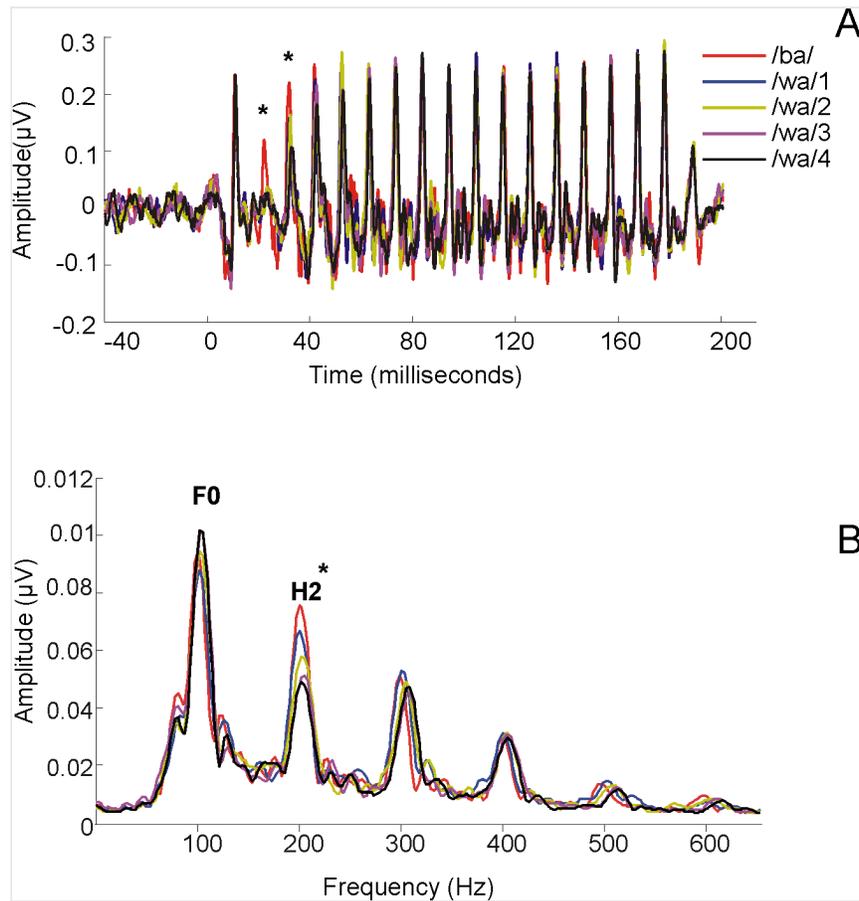


Figure 1. The Frequency Following Response (FFR) (A) and its corresponding spectra components (B) for the /ba/, /wa/1, /wa/2, /wa/3, /wa/4 stimuli presented with equal probability in

the same stimulus sequence. A) Notice the significant enhancement of the response amplitude in two latency windows (18-22 ms and 27-31 ms) over the temporal transition of F1 and F2 that was observed for the /ba/ syllable in comparison to the /wa/1 syllable ('*', $p < 0.05$). B) Remarkably, the amplitudes of the H2 harmonic followed the increase of the formant transition durations, so it can be considered as the biological marker of the encoding of this sound feature in the human auditory brainstem. Adapted from Slabu et al. (2012).

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Attention capture and orienting response

Attention is the cerebral function that allows one to keep all the processing resources in the information relevant for the task at hand --and in this regard it shares several relevant properties with working memory--, while at the same time keeps track of all potential relevant stimuli outside the current focus of activity. Hence, since the old times of scientific psychology two orthogonal forms of attention have been put forward (James, 1890): active selection or focused attention, and the breakthrough of the unattended (passive attention). The first is a top-down process, in which channels of information are selected or rejected under the direction of the central mechanisms of behavior (executive) control. The second is a bottom-up process that enables the conscious evaluation of those potentially relevant events falling outside the current focus of conscious attention. For example, it was long ago observed that participants could notice changes in the voice delivering an unattended speech message to one ear while attending to the speech message presented to the opposite ear, in what is known as the cocktail-party effect (Cherry, 1959). Obviously, a good balance between these two forms of attention is necessary. If the top-down processes dominate one's attention, one may not react to vitally important events. On the other hand, if bottom-up processes can too easily catch one's attention, then purposive behavior is fragmented, making goal-directed actions less effective. Years of functional neuroimaging research have confirmed the existence of these two separated, although closely related form of attention and have characterized the underlying supportive neural networks (Corbetta and Shulman, 2002; Corbetta et al., 2008). This partially segregated set of brain regions includes parts of the intraparietal cortex and superior frontal cortex in organizing goal-directed (top-down) selection for stimuli and responses, whereas a right dominant temporoparietal cortex and inferior frontal cortex network is specialized for the detection of behaviorally relevant stimuli, particularly when they are salient or unexpected (bottom-up).

The auditory system plays a particular key role in involuntary attention, as it can track sound sources at very long distances and those that fall quite outside the visual field, implementing mechanisms that can awake the individual from sleep for loud, unexpected or significant sounds (e.g., own baby's cry). Involuntary attention shifts in the auditory system were originally explained by the orienting-reflex theory (Sokolov, 1963), which posits that a neural model is built from the repetitive features of the

external environment. Subsequent research has identified at least two independent mechanisms by which involuntary attention can occur: According to Näätänen's model of attention, abrupt stimulus onsets and offsets activate a transient-detector mechanism, which is triggered by the surge in neural activity of silent neural populations that encode the features of the novel stimulus (Näätänen, 1992). On the other hand, the model also proposes another mechanism that relies on the encoding of the acoustic regularity and the issuing of an attention capture signal triggered by a mismatch between the afferent stimulus and the neural representation of the preceding regularity.

As introduced above, a large body of evidence has confirmed that the two mechanisms just outlined indeed operate in the auditory system. This evidence is based in the use of the so-called distraction paradigms, in which the participant has to discriminate between two categories of auditory or visual stimuli, while ignoring concurrent task-irrelevant sounds (see reviews in Escera et al., 2000; Escera and Corral, 2007). In all these experiments, the occurrence of an even subtle and minor change in any of the acoustic features of the ongoing auditory stimulation, as well as the occurrence of much more intrusive, novel environmental sounds (such as a telephone ringing), impaired task performance and delayed response times to the targets. In addition, these distracting sounds elicited a characteristic pattern of neural events that can be isolated in the electroencephalogram (EEG), the so-called distraction potential (DP; see Figure 2), and that reflect three successive stages in the involuntary attention chain. First, at about 100-150 ms from distracter onset, a mismatch negativity (MMN) can be observed, reflecting the detection of the disparity between the incoming signal and the memory trace of the preceding regularity (Escera et al., 1998; see above). Subsequently at circa 250-300 ms, a large positive potential is elicited, the so-called P3a or novelty-P3, which reflect the effective orienting of attention towards the eliciting sounds (Escera et al., 1998). At a later restoring stage, a reorienting negativity (RON) is observed, reflecting the returning of attention towards primary task performance after a transitory attention switch (Schröger and Wolff, 1998; Escera et al., 2001). All these event-related brain responses provide a very convenient model to investigate the mechanisms and processes of involuntary attention, as they can track with a millisecond accuracy the dynamics of the attention control network. Moreover, they have proved successful to reveal the interactions between top-down and bottom-up forms of attention, such as during

working memory load (SanMiguel et al., 2008) and emotional challenge (Domínguez-Borràs et al., 2009). As discussed above, it is very likely that, by the nature of the manipulations it introduces to the voice of users, **Forbrain**® induces a remarkable challenge to this cerebral network for involuntary attention control, and the recording of this involuntary attention-related potentials provides an unprecedented framework to validate its principles of action.

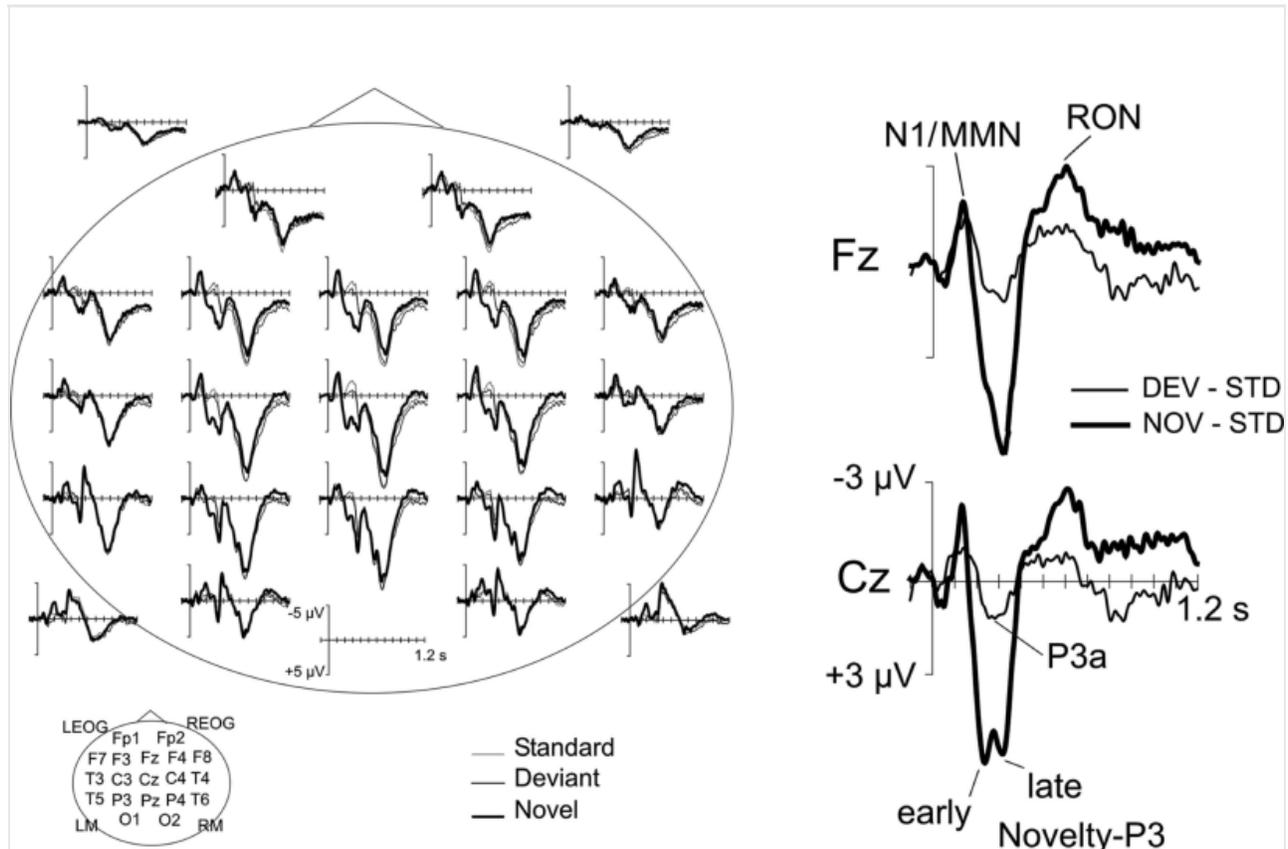


Figure 2. The distraction potential (DP). (left) Event-related brain potentials elicited to standard, deviant, and novel trials during visual task performance while ignoring the auditory stimulation. (right) Subtraction waveforms (distracting, i.e., deviant and novel, minus standard trials) revealing DP.

The DP appears as a three-phasic waveform disclosing the contribution of MMN, N1-enhancement, P3a/novelty-P3, and RON. Adapted from Escera and Corral (2007).