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Research Report

Electrical stimulation of the dorsal cochlear nucleus induces hearing in rats

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ABSTRACT

Auditory brainstem implants (ABIs) restore hearing by electrical stimulation of the cochlear nucleus (CN). Depending on the physiological condition, duration of the pre-existing deafness, extent of damage to the CN, and the number of channels accessible to the tonotopic frequency gradients of the CN, ABIs improve speech understanding to varying degrees. Although the ventral cochlear nucleus, a mainstream auditory structure, has been considered a logic target for ABI stimulation, it is not yet clear how the dorsal cochlear nucleus (DCN) contributes to patients' hearing during ABI stimulation. To better understand the mechanisms underlying ABIs, we tested if electrical stimulation of the rat DCN induces hearing using a novel electrical prepulse inhibition (ePPI) of startle reflex behavior model. Our results showed that bipolar electrical stimulation of all channels in the DCN induced behavioral manifestation of hearing and that electrical stimulation of certain channels in the DCN induced robust neural activity in auditory cortex channels that responded to acoustic stimulation and demonstrated well-defined frequency tuning curves. This suggests that the DCN plays an important role in electrical hearing and should be further pursued in designing new ABIs. The novel ePPI behavioral paradigm may potentially be developed into an efficient method for testing hearing in animals with an implantable prosthesis.

1. Introduction

Central auditory prostheses restore hearing by bypassing the cochlea and directly stimulating auditory brain structures. The auditory brain structures that are used as stimulation targets include the cochlear nucleus (CN; Cervera-Paz and Manrique, 2007; Colletti et al., 2000; Colletti et al., 2005; Colletti and Shannon, 2005; Edgerton et al., 1982; Evans et al., 1989; House and Hitselberger, 2001b; Kuchta et al., 2004; Laszig et al., 2004; Laszig and Aschendorff, 1999; Manrique et al., 2008; McCreery et al., 2007; McCreery, 2008; Otto et al., 2002; Schwartz et al., 2008; Shannon and Otto, 1990; Shepherd and McCreery, 2006; Takahashi et al., 2005) or the inferior colliculus (Colletti et al., 2007; Lenarz et al., 2007; Lenarz et al., 2006b; Lenarz et al., 2006a; Lim et al., 2008b; Lim et al., 2008a; Lim et al., 2007). The working principles are based on cochlear

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Abbreviations: ABI, auditory brainstem implant; AC, auditory cortex; aPPI, acoustic prepulse inhibition; BBN, broadband noise; CF, characteristic frequency; CIC, central nucleus of the inferior colliculus; CN, cochlear nucleus; DCN, dorsal cochlear nucleus; ePPI, electrical prepulse inhibition; FTC, frequency tuning curve; PPI, prepulse inhibition; VCN, ventral cochlear nucleus

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implants, which are implanted in the cochlea and convert acoustic signals to electrical impulses through a speech processor. The coded electrical signals are then forwarded to the implanted electrodes to directly stimulate the residual viable auditory nerve, thus bypassing the malfunctioning organ of Corti. However, when anatomical and functional abnormalities occur to the cochlea or auditory nerve, hearing loss will become inevitable. The auditory nerve often loses function during surgical removal of bilateral eighth nerve tumors in patients with neurofibromatosis type 2. Other functional abnormality in the cochlea or auditory nerve includes cochlear or cochlear nerve avulsion, cochlear aplasia, cochlear ossification, cochlear fracture, as well as damaged cochleas and/or cochlear nerves following head injuries. In any one of the above cases, the benefit of cochlear implants is severely compromised (Colletti et al., 2005; Colletti and Shannon, 2005; Moller, 2006; Shepherd and McCreery, 2006). Under these circumstances, central auditory prostheses are needed to restore hearing.

The most common form of central auditory prosthesis is auditory brainstem implants (ABIs), in which electrodes are implanted in or adjacent to the CN. ABIs evolved from a single electrode that resulted in partial recovery of hearing (Edgerton et al., 1982; McElveen, Jr. et al., 1985) to a multichannel surface or penetrating ABI system (Nucleus 24® ABI). In the Nucleus 24® surface system, a nearly rectangular electrode array carries 21 electrodes, which are arranged in 3 rows. The array consists of 0.7-mm platinum disk electrodes aligned on a flexible silicone and mesh backing. The electrode array is placed in the lateral recess of the fourth ventricle, making partial contact with the surface of the ventral cochlear nucleus (VCN) and the dorsal cochlear nucleus (DCN). Although there are improvements in speech understanding, the performance with Nucleus 24® ABI is generally poorer than with multichannel cochlear implants (Di Nardo et al., 2001; McCreery, 2008; Schwartz et al., 2008). In addition, the variability in speech performance is very high. For instance, the open-set sentence recognition scores 6–8 months after ABI activation ranged from 0% to 100% in adults (Colletti et al., 2004). It has been thought that the large variability in performance may be related to the duration of the pre-existing deafness, surgical removal of tumor from the brainstem, and the number of channels accessible to the tonotopic frequency gradients of the remaining CN (Colletti and Shannon, 2005; Di Nardo et al., 2004). Therefore, it is necessary to develop effective strategies in order to optimally stimulate patients' residual and viable CN tissue.

To achieve optimal results by maximally stimulating different portions of the CN, there is a need to understand how different parts of the CN contribute to speech perception following electrical stimulation using ABIs. Thus far, several investigations support the theory that ABI-induced speech perception is from electrical stimulation of the VCN (McCreery et al., 2007; McCreery, 2008; Schwartz et al., 2008), a primary auditory structure that executes phase-locked temporal processing of auditory information (Brugge et al., 1978; Rhode and Kettner, 1987). Information from animal studies has demonstrated that the VCN carries a high degree of frequency specificity to the inferior colliculus when stimulated electrically (Shivdasani et al., 2008). There is no question that the VCN plays a significant role in relaying electrically coded information from the speech processor to higher level auditory structures. In parallel, the DCN plays an important role in the processing of complex sounds, enhancement of behaviorally important auditory stimuli in changing and noisy environments, and in filtering sound localization cues (Portfors and Roberts, 2007; Zhao and Liang, 1997; Zhao and Liang, 1996). Anatomically, the DCN sends projections to the contralateral inferior colliculus via its dorsal acoustic stria (Cant and Benson, 2003; Cant and Benson, 2008; Osen, 1972; Ryugo and Willard, 1985). There is also direct projection to the medial division of the medial geniculate body, possibly modulating auditory information processing (Malmierca et al., 2002). In addition to the ascending projections to higher level structures, the DCN forms a feed-forward circuit projecting to the VCN by a tuberculoventral tract probably providing an inhibitory fringe (side bands) surrounding the center bands of the main ascending pathway (Alibardi, 2006; Munirathinam et al., 2004; Ostapoff et al., 1999). The DCN is also a polysensory structure upon which multimodal input converges to the auditory system (Benson and Brown, 1990; Caicedo and Herbert, 1993; Haenggeli et al., 2005; Itoh et al., 1987; Li and Mizuno, 1997; Ohlrogge et al., 2001; Schofield and Coomes, 2006; Weedman and Ryugo, 1996; Zhou et al., 2007). This makes the DCN a feasible site to conduct strong temporal processing of complex sounds instead of simple sounds (Zhao and Liang, 1997; Zhao and Liang, 1995; Zhao and Liang, 1996). However, thus far there is very limited published literature demonstrating the function of electrical stimulation of the DCN and how electrical stimulation of the DCN contributes to hearing in ABIs.

We set out to test whether electrical stimulation of the DCN yields hearing using a rat model. To achieve this goal, we developed a behavioral testing method based on an unconditioned electrical startle reflex paradigm. The background of this concept was that animals' hearing may be examined using unconditioned paradigms such as reflex orienting responses (Sutherland et al., 1998) and the acoustic prepulse inhibition (aPPI) startle reflex (Ouagazzal et al., 2006). In the aPPI paradigm, animals' startle responses are inhibited by hearing a preceding acoustic stimulus, which yield psychophysical results that are comparable to those obtained from operant paradigms (May et al., 2004; Su et al., 2008). In addition, compared to other conditioned behavioral paradigms such as T-maze (Paolini et al., 1998), suppression/avoidance procedure (Koay et al., 2002), and operant conditioning procedure (May et al., 2004; Su et al., 2008), the aPPI paradigm takes much less time to complete. In the present study, to examine whether animals hear electrical stimulation, we used a short train of electrical pulses to substitute for the acoustic prepulses in the aPPI paradigm, creating an electrical PPI (ePPI) paradigm. This idea is also supported by a previous study showing that electrical stimulation of the VCN elicits hearing and causes startle-like responses (Davis et al., 1982). However, ePPI paradigm has not been used to test hearing following electrical stimulation of the DCN. Since this paradigm takes less time to obtain psychophysical reports compared to the available conditioned behavioral methods in cochlear implants research (Beitel et al., 2000; Su et al., 2008; Vollmer et al., 2001), there is a potential that this behavioral paradigm could be developed into a highly efficient method for testing hearing of animals with an