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Speech sound training alters auditory processing in rats

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ABSTRACT

Speech sounds evoke unique neural activity patterns in the primary auditory cortex (A1) of rats. Like humans, rats can easily learn to discriminate between speech sounds. Behavioral discrimination accuracy can be predicted by the neural similarity of the A1 response pattern to pairs of speech sounds. For example, pairs of sounds that evoke very similar A1 activity patterns are difficult for rats to discriminate, while pairs of sounds that evoke very distinct A1 activity patterns are easy for rats to discriminate. Rat models of autism exhibit many of the classic neural and behavioral deficits observed in individuals with autism. Extensive speech discrimination training alters auditory cortex responses in both experimentally naïve rats and in rat models of autism. However, in some autism models, training alone is insufficient to reverse neural processing deficits. Vagus nerve stimulation (VNS) triggers rapid, phasic release of plasticity promoting neuromodulators, which enhances plasticity in the auditory network when delivered with sound presentation. For example, pairing the sounds 'rad' and 'lad' with VNS increases the A1 response strength to the paired sounds. Ongoing work involves pairing VNS with auditory training in rat models of autism to improve both sound discrimination ability and the neural processing of sounds.

Keywords: Auditory processing, Vagal nerve stimulation, Autism

1. THE NEURAL AND BEHAVIORAL PROCESSING OF SPEECH SOUNDS IN RODENTS

1.1 Behavioral discrimination of speech sounds

Like humans, rodents can easily learn to discriminate between speech sounds (1–4). For example, in one of the most well-known studies of animals discriminating human speech sounds, chinchillas were successfully trained to categorize the consonant /d/ from the consonant /t/ in multiple talker and vowel contexts (1). Since then, numerous animals have been shown to accurately categorize these sounds. Gerbils were trained to categorize speech sounds into vowel, liquid, or stop consonant categories (5). Rats were able to use differences in the rise time cue in order to discriminate between the affricate 'ch' and the fricative 'sh' (6). In fact, rats are able to discriminate between most English consonant and vowel sounds (3,4,7,8). While consonants that are acoustically distinct, such as /d/ and /s/, are easy for rats to discriminate, as consonants become more acoustically similar, discrimination accuracy decreases. Rats have difficulty successfully discriminating between the consonants /r/ and /l/, as well as between the consonants /m/ and /n/ (Figure 1).

Also like humans, rats can discriminate speech sounds in a variety of difficult listening conditions. Rats can discriminate speech sounds in the presence of background noise, as well as after varying levels of spectral or temporal degradation (9,10). In addition to being able to discriminate between individual consonant and vowel sounds, rats are able to perform more complex speech discrimination tasks. For example, rats can discriminate between sentences spoken in Dutch versus sentences spoken in Japanese (11). Additionally, rats can detect syllable regularities within a speech stream (12–14). Rats are also able to generalize a rule to novel words differing in voicing or in the gender of the speaker (15). These studies documented that the mammalian auditory system is highly effective at discriminating between the basic elements of human speech sounds, and paved the way for numerous studies using rats as a model of speech processing.

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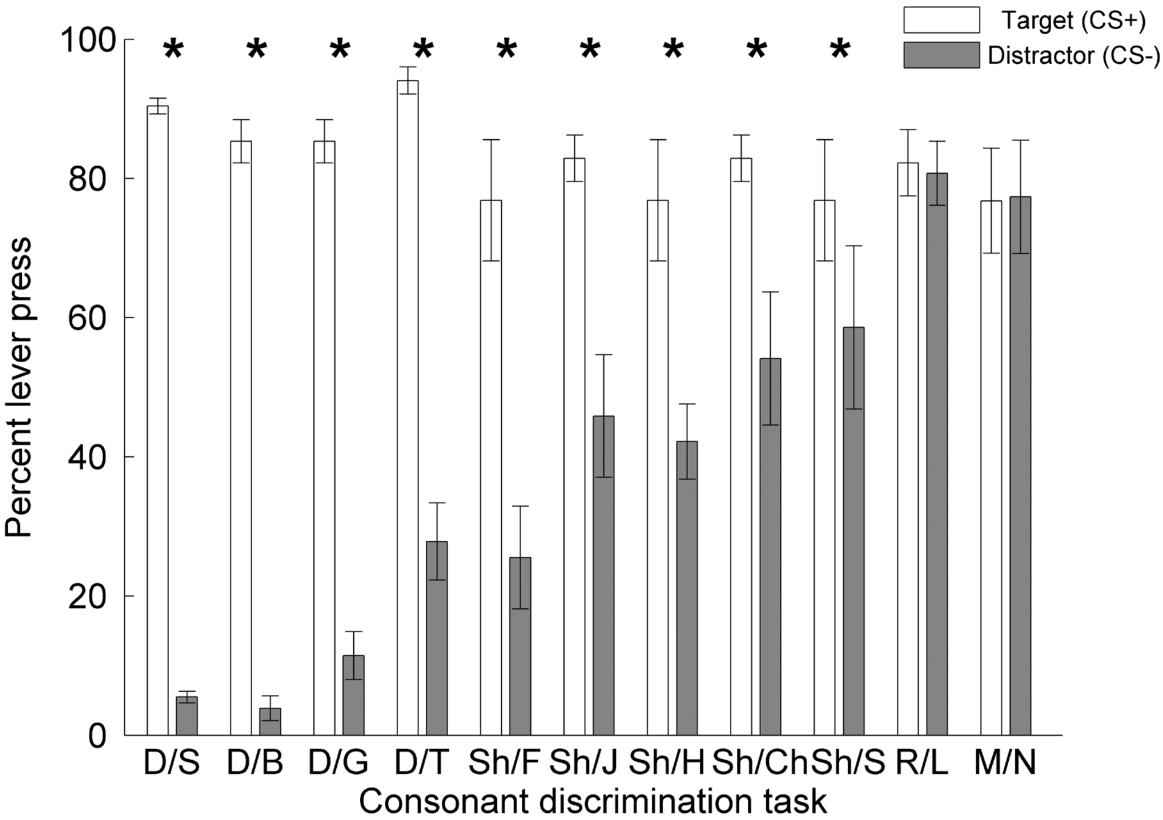

Figure 1. Behavioral discrimination accuracy of consonant sounds. Rats successfully discriminated nine of eleven consonant pairs evaluated. Open bars represent the target sound for each go/no-go task and filled bars represent the non-target (distractor) sound. Error bars indicate s.e.m. across rats. Asterisks indicate significant discrimination between the target and non-target consonant sounds. Reproduced from (3) with permission.

1.2 Neural representation of speech sounds

Early in the auditory pathway, neural responses to speech sounds closely resemble the physical characteristics of the sound, while at higher levels of the auditory pathway, the neural responses grow more abstract to better represent the perceptual characteristics of the sound (4,16). Each speech sound evokes a unique neural activity pattern in the primary auditory cortex of animals (3,16,17). For example, the consonant /s/ has high frequency acoustic energy, which evokes neural activity from neurons tuned to high frequencies, while the consonant /r/ has low frequency energy, which evokes neural activity from neurons tuned to the low frequencies. In addition to spectral differences in the neural response pattern to speech sounds, there are also temporal differences. While voiced stop consonants (such as /d/) evoke a single peak of activity in response to the consonant onset, voiceless stop consonants (such as /t/) evoke a peak of activity in response to the consonant onset and a second peak of activity in response to the subsequent vowel onset.

Behavioral discrimination accuracy can be predicted by the neural similarity of the A1 response pattern to pairs of speech sounds. Pairs of sounds that evoke very similar A1 activity patterns are difficult for rats to discriminate, while pairs of sounds that evoke very distinct A1 activity patterns are easy for rats to discriminate. For example, the consonants /r/ and /l/ evoke very similar neural patterns of activity, and are difficult for rats to behaviorally discriminate. On the other hand, the consonants /d/ and /s/ evoke very distinct neural patterns of activity, and are easy for rats to discriminate. Interestingly, consonant and vowel sounds are processed distinctly. While precise neural spike timing information is required to accurately identify consonants, only the average neural spike rate is required to accurately identify vowels (4). Neural activity from four cortical auditory fields and one subcortical auditory field can be used to accurately predict behavioral speech discrimination ability (3,4,18).

2. AUDITORY PROCESSING DEFICITS IN RODENT MODELS OF AUTISM

Unfortunately, individuals with autism spectrum disorders often exhibit degraded neural responses to sounds and impaired speech perception abilities (19,20). Rodent models of autism exhibit many of the classic neural and behavioral deficits observed in individuals with autism (21–24). For example, rodents that were prenatally exposed to valproic acid (VPA) exhibit weaker and delayed auditory cortex responses to sounds (21,22,25). VPA-exposed rats also are impaired at discriminating between words varying in initial consonant, although their ability to discriminate between vowel sounds remains intact (26).

Similarly, individuals with Rett syndrome have impaired receptive language and significantly degraded cortical responses to sound (27–30). Rodents with heterozygous *Mecp2* mutation, which models Rett syndrome, also exhibit alterations in the auditory cortex response to sounds (23,24). These rats accurately discriminate speech sounds in a quiet background, but have impaired discrimination accuracy when the speech sounds are presented in the presence of varying levels of background noise. These rodent models of the auditory processing deficits observed in autism spectrum disorders could easily be used to test the effectiveness of potential adjunctive intervention therapies.

3. SPEECH TRAINING IMPROVES AUDITORY PROCESSING

Extensive speech discrimination training alters performance accuracy and auditory cortex responses in both experimentally naïve rats and in rat models of autism. Speech sound training in experimentally naïve rats alters the neural response to sounds in multiple auditory cortical areas (31). Weeks of training in VPA-exposed rats improves consonant discrimination performance (26). This training also strengthens responses in anterior auditory field and decreases the neural response latency to sounds (Figure 2). This finding mirrors the improved behavior and normalized neural responses observed following extensive intervention in individuals with autism.

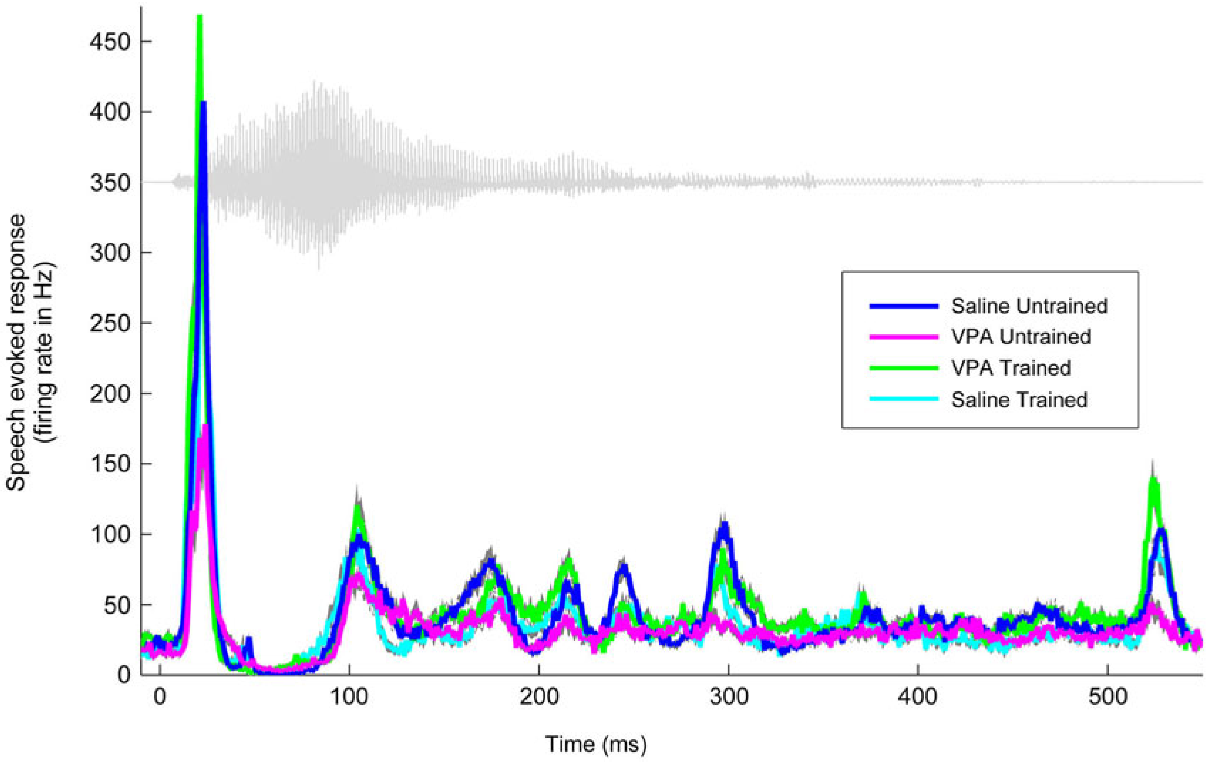

Figure 2. Speech training enhances the neural response to the speech sound "gad". The weakened response to "gad" in AAF in VPA-exposed untrained rats (n = 11 rats; magenta line) is normalized in VPA-exposed speech trained rats (n = 5 rats; green line), and is compared to saline-exposed untrained rats (n = 6 rats; blue line) and saline-exposed speech trained rats (n = 4 rats; cyan line). Reproduced from (26) with permission.

However, in some autism models, training alone is insufficient to reverse neural processing deficits. While heterozygous *Mecp2* rats are able to accurately discriminate consonant sounds before the onset of regression, discrimination performance is greatly impaired following regression onset and the onset of seizures. Extensive training in heterozygous *Mecp2* rats improves speech-in-noise discrimination performance (24). However, this training does not improve neural responses to sounds, and neural plasticity in these rats was abnormal. The development of enhanced therapeutic interventions is needed in order to increase the benefit of rehabilitative therapies for individuals who undergo these interventions and still experience deficits.

4. VNS-SOUND PAIRING IMPROVES AUDITORY PROCESSING

Vagus nerve stimulation (VNS) triggers rapid, phasic release of plasticity promoting neuromodulators, which enhances plasticity in the auditory network when delivered with sound presentation. For example, pairing VNS with a 9 kHz tone increases the proportion of A1 that responds to the paired tone frequency (32–36). Pairing VNS with fast or slow trains of tones can increase or decrease the A1 response strength to rapid sounds (37). Similarly, pairing the sounds 'rad' and 'lad' with VNS increases the A1 response strength to the paired sounds (38). Pairing VNS with speech sounds alters auditory cortex responses to a greater degree and alters responses significantly faster than speech training.

VNS paired with sound presentation has also been used to restore auditory processing in a rat model of tinnitus (32). Noise trauma rats were exposed to 115 dB noise centered at 16 kHz for one hour. One month later, neural effects were quantified using auditory brainstem responses and the behavioral correlate of tinnitus was determined using the Turner gap detection method (39). Rats then received daily VNS-tone therapy sessions, where VNS was paired with multiple tone frequencies that were distinct from the perceived tinnitus frequency. One month of VNS-tone pairing sessions reversed both the behavioral and neural effects of noise exposure. Current experiments are examining VNS-sound pairing in rodent models of autism with degraded auditory processing.

5. CONCLUSIONS

Speech sounds evoke unique patterns of neural activity, and rats can accurately discriminate between these sounds. Many rodent models exhibit degraded auditory processing. Speech training can improve neural and behavioral auditory processing in some rat models, but can be insufficient to restore auditory processing in other models. Ongoing work involves pairing vagus nerve stimulation with auditory training in rat models of autism to improve both sound discrimination ability and the neural processing of sounds.

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