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To the Brain and Back: A Potential Role for GABA in Speech-In-Noise Perception and Aging

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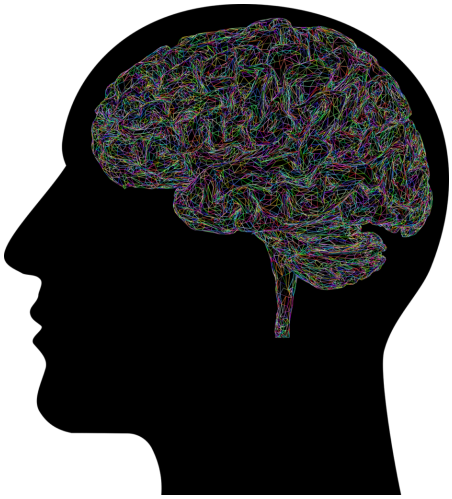

Audiologists frequently receive complaints from older adults with hearing loss about their difficulty understanding speech in noise (SIN). Sensorineural hearing loss is the primary reason for this problem, but SIN deficits can persist even with hearing aid use. As a result, clinicians and researchers have long suspected that there could be age-related problems with how the brain processes sound, separate from sound coding problems arising from inner ear damage. As the brain ages, there are changes to its structure and function that could impede a listener's ability to separate speech features from background noise. What are these changes, and how does this knowledge inform audiological practice?

In this article, I will highlight recent research that examines age-related changes in *neural inhibition* in older adults' brains and how these changes could impact SIN perception. Neural inhibition refers to active reductions in the excitability of neurons or populations of neurons and involves neurotransmitters that suppress neuronal activity. Excitation and inhibition must be in the right balance to ensure smooth nervous system operation. Too much excitation makes the brain hyperactive, and neural communication becomes noisy and imprecise. With too much inhibition, neurons may become unresponsive.

Many older adults show evidence of changes to the excitation–inhibition balance, often showing less inhibition and more excitation. Lower neural inhibition has been a candidate explanation for general functional decline in aging, impacting movement, memory, and other areas of cognition (Levin et al., 2014; McQuail et al., 2015). One major neurotransmitter involved in inhibition is gamma-aminobutyric acid, or GABA. With more GABA, there is more neural inhibition. GABA levels decrease in many parts of adults' nervous systems with aging (Gao et al., 2013), including

the auditory cortex (Gao et al., 2015). If GABA reductions are linked to general functional decline with aging, could it also contribute to age-related SIN difficulty?

At Baycrest Hospital in Toronto, Dobri and Ross (2021) set out to address this question in a study with 19 older (average age ~77 years) and 19 younger (~24 years) adults, who each underwent pure-tone audiometry and the QuickSIN test to measure speech-in-noise loss. GABA levels in the auditory cortex were estimated using Magnetic Resonance Spectroscopy, a noninvasive technique that measures concentrations of metabolites in neural tissue. Consistent with past research, Dobri & Ross (2021) found that older adults had lower GABA levels in left and right auditory cortex than younger adults. With the increasing age of the older group, GABA further decreased. These results agree that older adults have less neural inhibition in the auditory system. With respect to SIN perception, older adults with lower QuickSIN scores had lower GABA levels in the right auditory cortex. This relationship was separate from age and hearing loss measured by audiometric pure tone averages. The findings suggest that lower auditory cortical GABA levels in aging could contribute to SIN difficulty, distinct from problems arising from the periphery.

It's important to note that these data are correlational. From this study alone, we cannot infer that reduced GABA *causes* SIN problems, but the findings strongly suggest that GABAergic inhibition is somehow implicated. In addition, the authors measured pure-tone average thresholds from 250 Hz to 4 kHz, however, these thresholds provide an incomplete picture of potential dysfunction in the inner ear due to aging. Thresholds above 4 kHz are correlated with SIN listening ability (Motlagh Zadeh et al., 2019), and thresholds for pure tones may miss problems with complex sound encoding at conversational speech levels that are well above the threshold (Bharadwaj et al., 2014). However, a similar study conducted by Harris and colleagues (2022) also measured GABA levels in older adults. Still, instead of the audiogram, it recorded Wave I of the auditory brainstem response to better capture peripheral deficits. Nonetheless, the data from Harris et al. (2022) and Simon and Dobri (2021) agree GABA levels provide additional information about SIN listening beyond peripheral factors alone, revealing a potential central mechanism behind age-related SIN declines.

The coordination of neural excitation and neural inhibition mentioned at the start of this article helps shape brain function by synchronizing *neural rhythms*. Rhythmic neural activity is ubiquitous across the nervous system, and the timing and coordination of neural rhythms are thought to underpin cognitive and perceptual processing. GABA inhibition helps to maintain temporal synchrony of neural rhythms. If GABA levels decline, we should see evidence that neural encoding of sound, especially in noise, is also disrupted.

This was the prediction by Dobri, Chen, and Ross (2023), a follow-up study with the same participants from Dobri & Ross (2021). The authors used magnetoencephalography (MEG) to measure neural encoding of sound. In particular, they recorded the 40 Hz Auditory Steady State Response (ASSR), which are neural rhythms elicited when a listener is presented with a tone that is amplitude modulated at a rate of 40 Hz (ASSRs can also be evoked using click trains). In other words, researchers present a pure tone that "flutters" in amplitude at a rate of 40 Hz. The result is a brain response that is synchronized, or entrained, to the 40 Hz stimulation rate. This is significant because 40 Hz neural rhythms arise from brain networks that are responsible for parsing and binding speech features into meaningful perceptions. How do these responses change with age and SIN perception?

Dobri, Chen and Ross (2023) found that the amplitude of the 40 Hz ASSR evoked in quiet was not

different between younger and older age groups. But when these responses were observed in noise, they were larger (i.e., more synchronous) in older adults compared to younger adults. One may think that larger ASSRs in older adults represent strong neural processing, but larger ASSRs occurred in older adults of higher age and with worse QuickSIN scores. This suggests that larger, more synchronous ASSRs reflect disrupted neural processing. More specifically, the authors speculated that the increased synchrony was due to the reduced ability to separate speech features from background noise. Does this relate to GABA inhibition? Using a statistical modeling technique, the authors found that GABA levels best explained why heightened neural synchrony related to worse SIN perception in older adults. In other words, lower inhibition reduced GABA may produce more excitable, synchronized neural activity, but this could introduce problems separating speech from background noise. Although these findings are exciting, further research is needed to understand the causal relationships between age, neural inhibition, synchrony of neural rhythms, and speech perception.

These studies suggest that reduced neural inhibition in the auditory cortex may contribute to a decline in speech-in-noise ability in older adults. What can we take away from this? First, this further supports the view that speech-in-noise problems partly arise from issues beyond the ear. Second, rehabilitation of SIN problems in older adults will likely require a multifaceted approach, such as combining hearing aid use with specialized training. For example, older adults who participated in a 10-week choral singing program improved SIN perception and neural responses to speech (Dubinsky et al., 2019). In addition, intact senses like vision may help to reestablish an excitation–inhibition balance for speech perception. Middle-aged and older adults trained on visual speechreading for three weeks show improvements in audiovisual speech in noise perception (Schmitt et al., 2023). Although these and other interventions are encouraging (see Gohari et al. 2023 for a review), there is no one-size-fits-all model. The challenge for researchers and audiologists is to develop various strategies that best fit patient needs cooperatively.

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