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Critique of "The Effect of Glycine Receptor α1 Subunit Blockage on Phase Locking in Cochlear Nucleus Bushy Cells" By Yang & Zhang

The paper has potential, but there are several bugs that need to be worked out. The Background mentions non-synchronized negative monotonic neurons in the CN, and then says "*If test subjects show conserved ability to detect these sounds, despite blocking of bushy cell glycine receptors, this could point to a possible use of these neurons, meriting further study.*" There isn't a detection task in the design however, only a recording of single neurons in the AVCN in response to clicking. This makes the study of the non-synchronized cells unlinked to the experiment at hand.

The hypothesis is not completely testable as is – this will be addressed further later on in the critique. It is hypothesized that, *"blockage of the glycine receptor in the bushy cell will lead to a decreased ability of the bushy cell to phase-lock to auditory signals due to a loss of inhibitory regulation,"* however it is unclear how the data will tell whether a cell can phase lock or not.

The experimental design seems confusing and somewhat unrealistic. First the authors say that macaques will be used because, *"broad tuning for interaural time differences (ITD) have been observed in awake cat and primates,"* but have not previously discussed what broad tuning is. If this tuning is referring to **frequency**, it would be appropriate for the authors to discuss why the subject should have 'broad tuning for ITD' in order for the experiment to be successful. Next it is stated that Strychnine will be used as an agonist. Agonists mimic the action of naturally occurring molecules that bind to receptors. The writer should use strychnine as an *antagonist*, which would block glycine receptor sub unit α-1, thus decreasing inhibition. Perhaps this is a typo.

Further, the micro-iontophoresis procedure is a bit confused. The authors posit that *"The type of cell being recorded will be deduced from the signaling received, as globular and spherical bushy neurons uniquely produce monotonic primary-like responses,"* this may be true, but it seems unfeasible to record cell by cell, blindly, until a bushy cell is found. The number of trials "n" is also unspecified. The author should state how many neurons should be recorded from (how many spherical bushy and how many globular bushy) in order to provide statistically significant data. The click stimulus conditions are confusing. First it says the clicks will be either broad OR narrow band. Then later it says clicks are optimal for bushy cell response "*due to their broadband frequency*." This seems to be in contradiction. The significance of the click conditions that were chosen is unstated.

The manner of data analysis is also not discussed. This is necessary because it is critical to the expected results section. As is, the authors say that the hypothesis with be substantiated or disproven by the status of synchrony (synchronized v. unsynchronized). This is vague. No direct link is made to indicate how the data gathered via extracellular recording translates to an interpretation of the cell as synchronous or unsynchrounous. How exactly do the responses to the various click conditions translate into data? That issue aside, the authors say that "*The hypothesis will be accepted if there is a decrease in phase locking ability in the bushy cell.*" For this to make sense, the design should include an initial condition before application of strychnine, to which the experimental condition can be compared, in order to see if there has been a decrease in phase locking ability.