

Angiotensin II and $-(1-7)$ concentrations in human hair samples reflect the degree of tinnitus-related distress

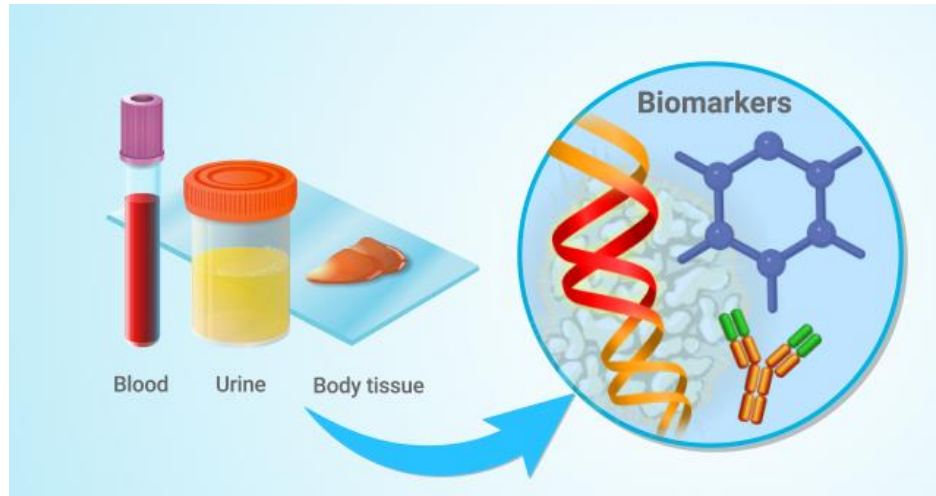
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Background

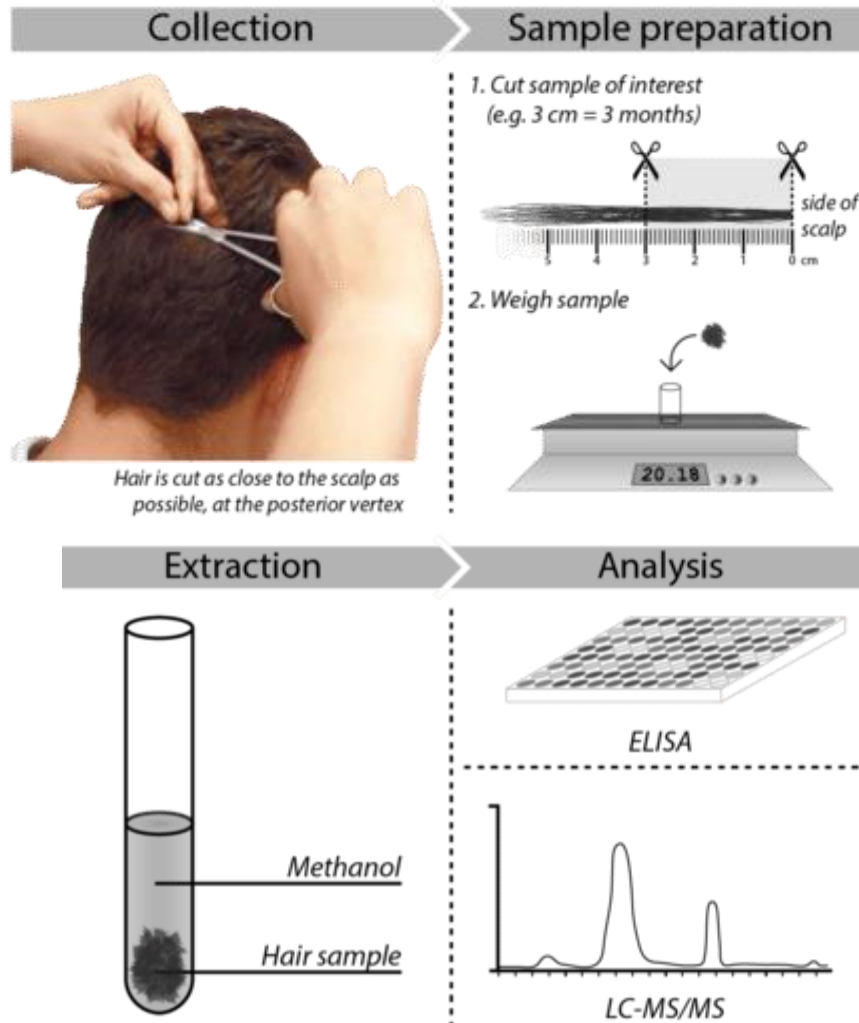
Tinnitus biomarkers



“Something, for example a gene or substance, that shows that a particular biological process or condition is present.” (Cambridge Dictionary)

- Tinnitus diagnosis and assessment largely based on audiometric and psychometric testing
- Both approaches susceptible to subjective bias and require active participation of the patient
- Hence, **biomarkers** that might enable a more objective assessment of tinnitus and associated **distress** would be useful
- No established markers yet, despite various attempts (e.g., cortisol and BDNF)

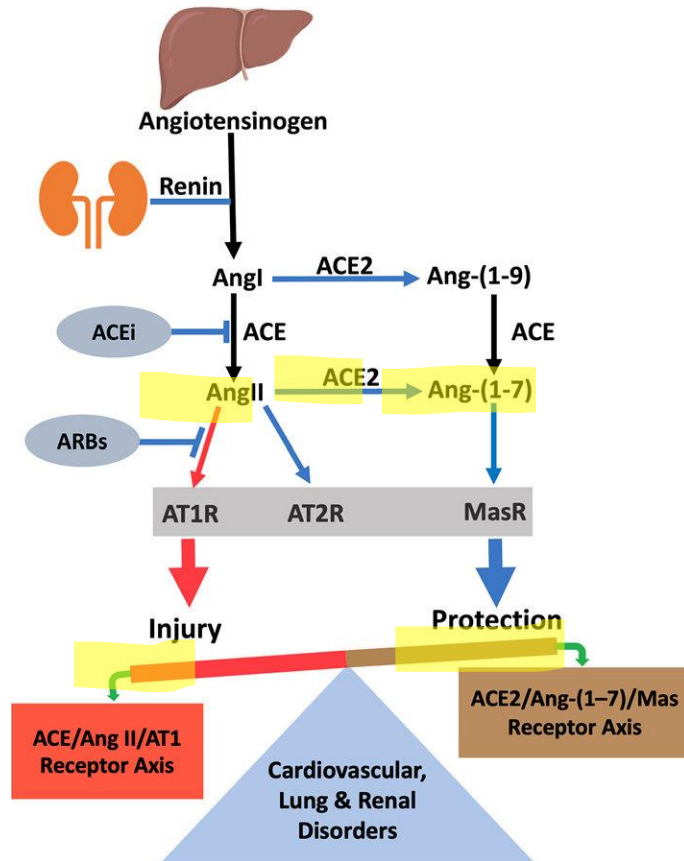
Tinnitus biomarkers



- For **cortisol**, saliva-based analyses showed lower concentrations in chronic tinnitus patients compared to controls (Hébert et al., 2007, 2009)
- However, no consistent findings for blood-based analyses of cortisol & BDNF (Haider et al., 2021)

- **Hair-based** analyses, in contrast, provide a mean for assessing long-term effects
- Yet, no clear-cut association of hair-cortisol and hair-BDNF with tinnitus distress either (Basso et al., 2022a, 2022b)

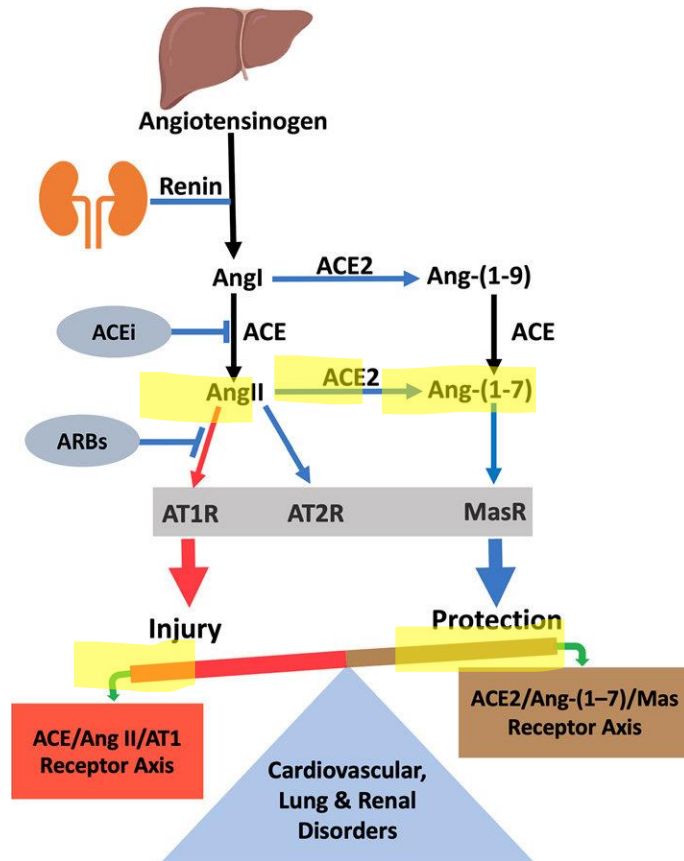
Angiotensin II and -(1-7)



Sharma et al., 2021
<https://doi.org/10.1042/CS20200482>

- The peptide hormone **Ang II** is the end-product of the renin-angiotensin system (RAS) originating in the kidneys and liver
- Ang II has long been known to induce vasoconstriction and thirst, thereby causing **hypertension**
- More recently, Ang II was also discovered to be **pro-inflammatory** and to promote stress

Angiotensin II and -(1-7)



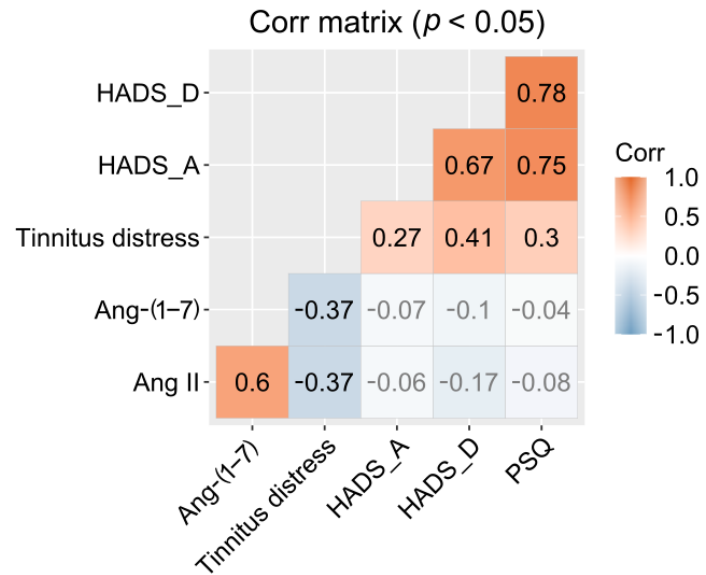
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- Ang II is converted into its **antagonist, the anti-inflammatory Ang-(1-7)**, via ACE2
- Renewed interest in ACE2-based conversion of Ang II into Ang-(1-7) during **COVID-19** pandemic, as virus binds to ACE2 to enter cells.
- *Here, we re-analysed hair samples of 80 patients before and after CBT intervention (i.e., long-term distress)*

2

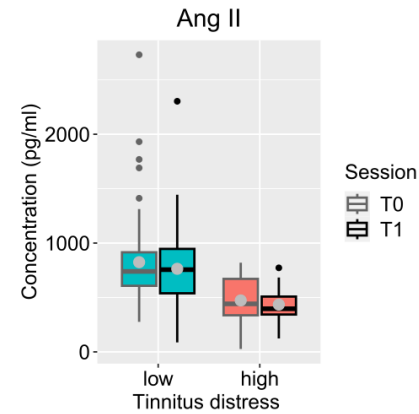
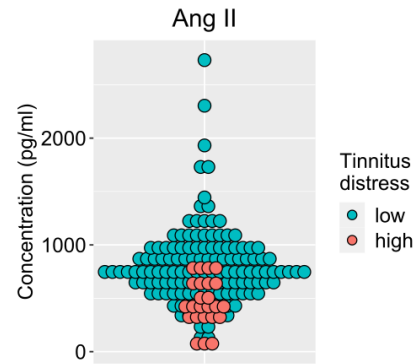
Results

Angiotensin and general distress



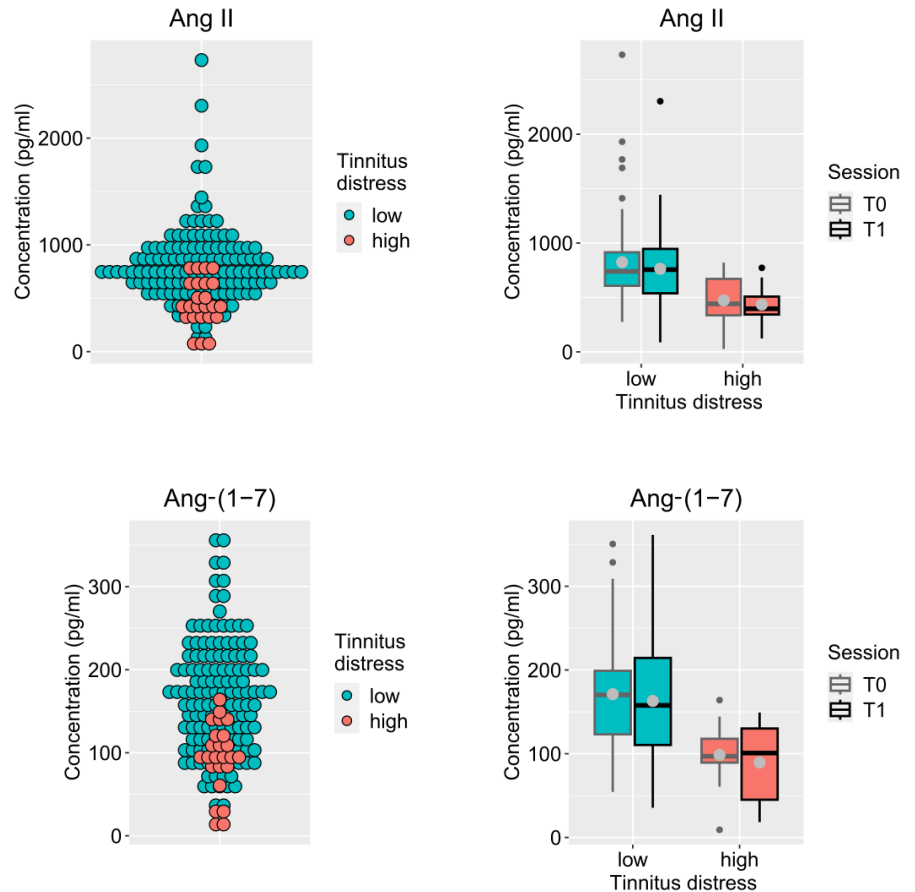
- Hair-angiotensin concentrations **unrelated** to general measures of distress (HADS, PSQ)
- Negative correlations of Ang II **and** -(1-7) with degree of tinnitus-related distress

Angiotensin and tinnitus distress



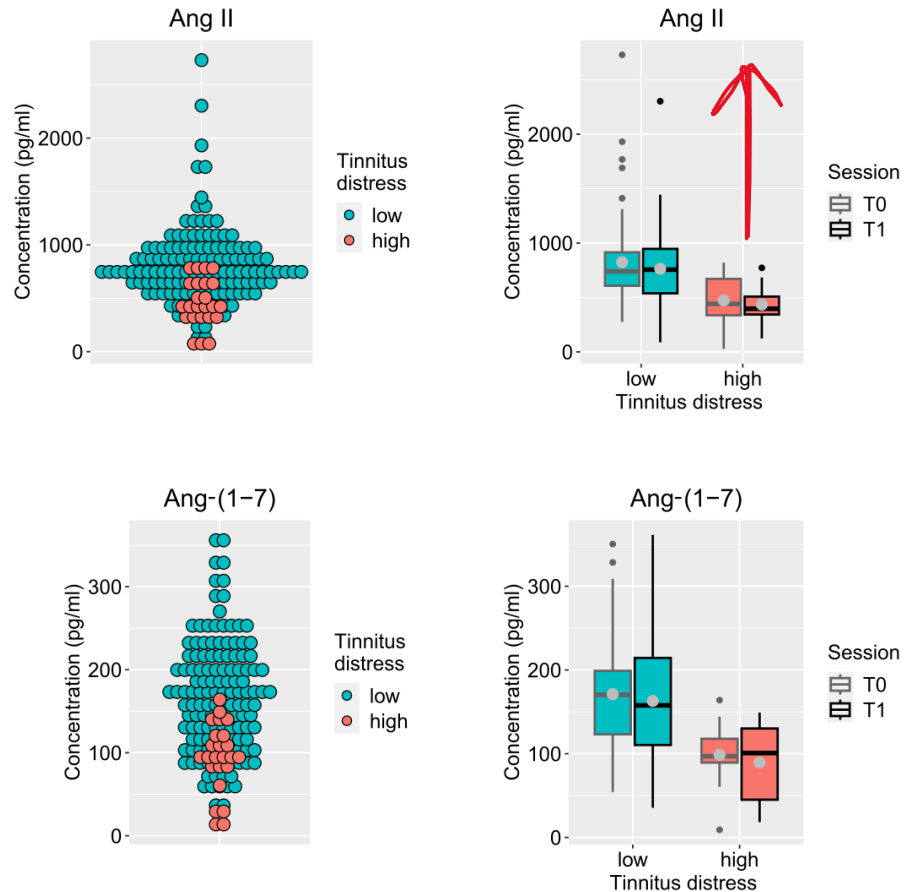
- Hair-**Ang II** concentration significantly **lower** ($p < 0.001^{***}$) in patients with a high degree of tinnitus-related distress
- No other significant predictors

Angiotensin and tinnitus distress



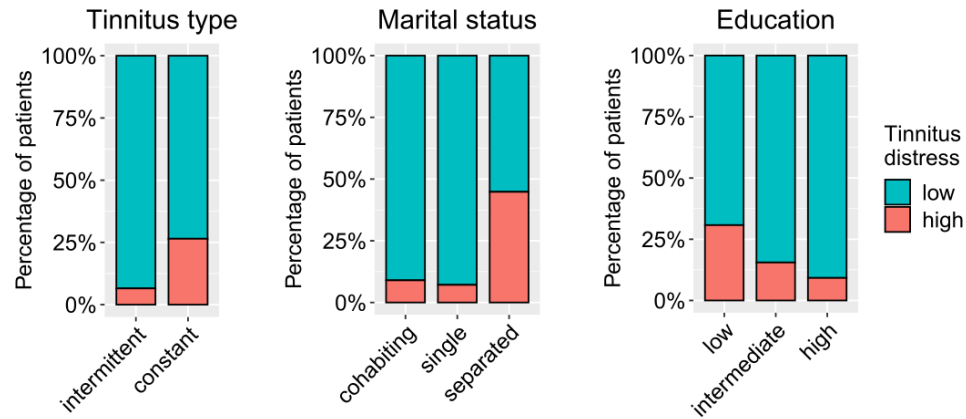
- Hair-**Ang II** concentration significantly **lower** ($p < 0.001^{***}$) in patients with a high degree of tinnitus-related distress
- No other significant predictors
- Exactly the same pattern ($p = 0.002^{**}$) for **Ang-(1-7)**
- Tinnitus type as only other significant predictor ($p = 0.028^*$): lower, if intermittent

Angiotensin and tinnitus distress



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- No other significant predictors
- Exactly the same pattern ($p = 0.002^{**}$) for **Ang-(1-7)**
- Tinnitus type as only other significant predictor ($p = 0.028^*$): lower, if intermittent
- *Based on literature, one would expect **higher** Ang II and **lower** Ang-(1-7) concentrations in case of higher tinnitus distress*

Angiotensin and tinnitus distress

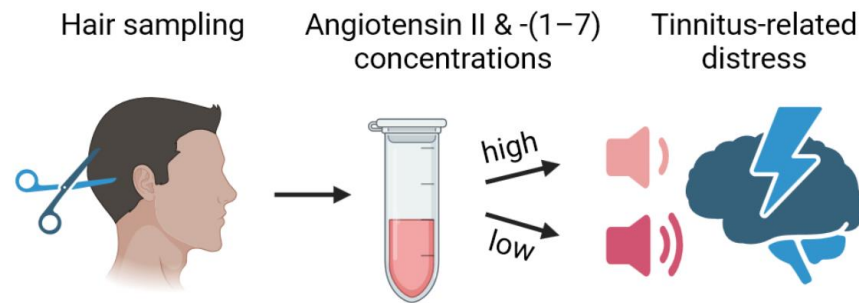


- Conversely, the summed **Ang II and Ang-(1-7)** score was the best predictors of the tinnitus distress level ($p=0.002^{**}$)
- Other significant predictors were:
 - the tinnitus type ($p=0.014^*$),
 - the marital status ($p=0.003^{**}$), and
 - the education level ($p=0.031^*$)

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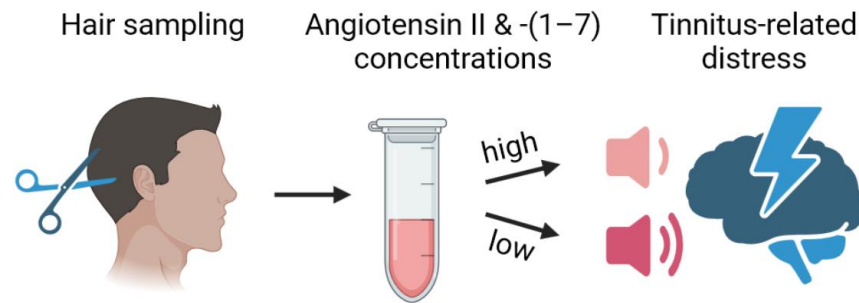
Summary and discussion

Summary and discussion



- First study to assess Angiotensin concentrations in human hair samples
- Results **specifically** reflect the degree of tinnitus-related distress, not the general stress level
- However, **direction of effect** for Ang II is at odds with the (rodent) literature! Higher tinnitus distress should result in higher Ang II levels

Summary and discussion



- Indeed, there are concerns that the applied ELISA methods measure **other immunoreactive substances** in addition to Angiotensin (Chappell, 2021)
- Further analyses (e.g., **mass spectrometry**) will be required to identify the exact substances/biomarkers underlying the observed effects

Thank you for your attention!



TINNITUS RESEARCH INITIATIVE CONFERENCE

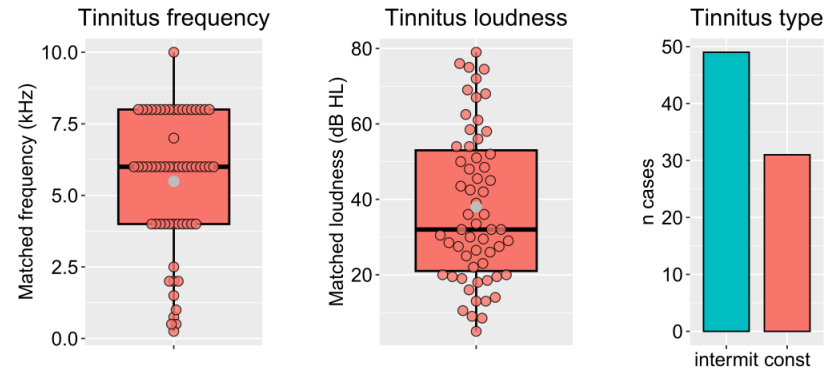
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Jump the wall – discover and uncover gaps

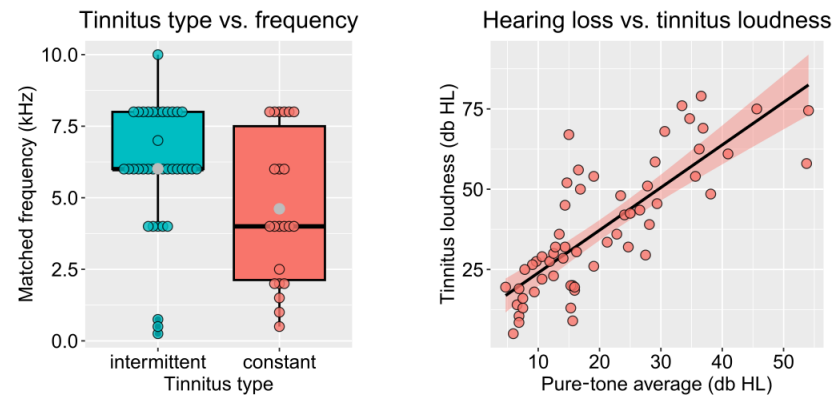
Appendix

Acoustic tinnitus characteristics

A

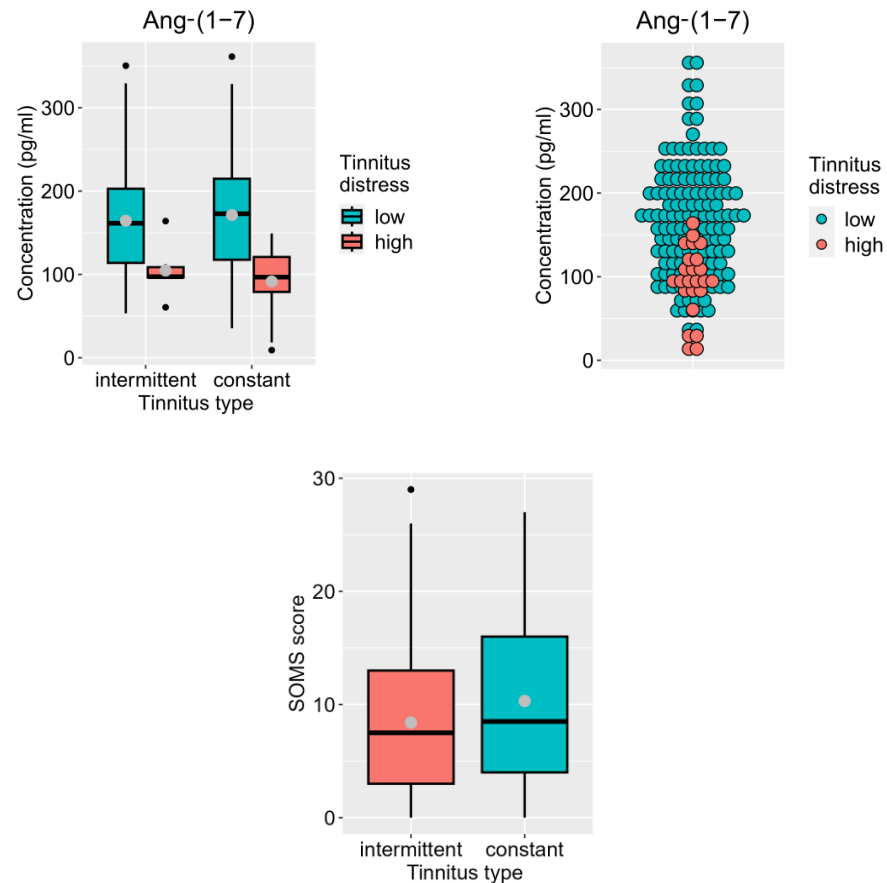


B



- Majority of patients indicated an intermittent as opposed to a continuous tinnitus (49/31)
- Matched tinnitus frequency significantly higher in patients with **intermittent tinnitus**
- Matched tinnitus loudness increased with higher pure-tone averages, i.e., a greater degree of hearing loss (**loudness recruitment**)

Intermittent tinnitus



- **Ang-(1-7)** concentration was **lower in patients with an intermittent tinnitus**

- This effect was driven by the subgroup with a low degree of tinnitus distress, which contained most patients.

- Higher SOMS scores in case of constant tinnitus ($p=0.018^*$)