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Neural Plasticity in the Visual Cortex of People with Visual Snow Syndrome

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Introduction. Visual Snow Syndrome

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- **Increased excitability** (Ghannam et al., 2017) is considered as one of the most likely causes for the development of the Visual Snow Syndrome (VSS)
- Alterations in neural plasticity have been proposed as potential pathophysiological mechanisms of VSS (Aldusary et al., 2020)

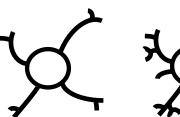


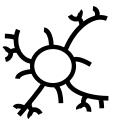
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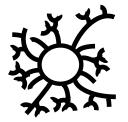
Introduction. Neuroplasticity and E/I Balance

 Neuroplasticity enables learning and adaptation through synaptic remodeling (Hebbian plasticity; Fries et al., 2007)

 Excitation/Inhibition (E/I) balance maintains neural stability and sensory processing by regulating excitatory and inhibitory activity (Sohal & Rubenstein, 2019)









Introduction. Gamma Oscillations as E/I Biomarker

- Gamma Response (GR) parameters are generated by E-I interactions (pyramidal-PV+ interneuron loops; Cardin et al., 2009)
- Moving gratings paradigm was suggested to characterize E/I balance (Orekhova et al., 2018)
- Gamma activity was demonstrated to be increased in VSS (Hepschke et al., 2022)

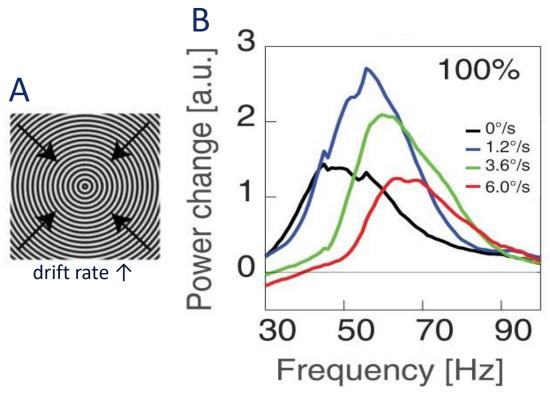


Figure 1. (A) Stimulus used in the study. (B) Grand average spectra of cortical GRs to the gratings of 100% contrast drifting at four motion velocities (Orekhova et al., 2020)

Introduction. Gamma Oscillations and Neuroplasticity

- Visual gamma oscillations recorded by MEG can reflect repetition-related neuroplasticity
- In Stauch et al. (2021) gamma power changes across stimulus repetitions were shown to be stimulus-specific and persistent for over 25 minutes
- Similar GR patterns in studies on monkeys (Brunet et al., 2014; Peter et al., 2021)

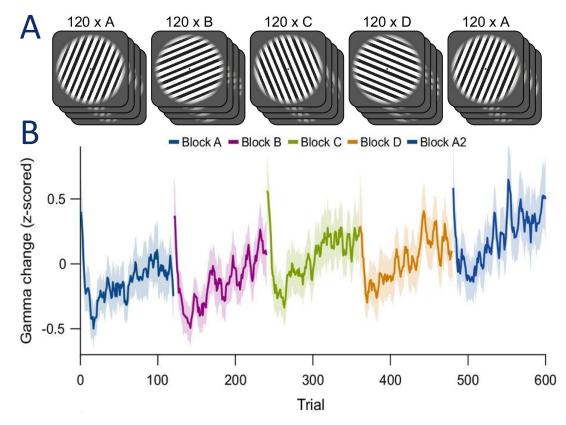


Figure 2. (A) Stimulus used in the study. (B) Stimulus-induced gamma power in V1/V2, on a per-trial basis for 5 recording blocks (Stauch et al., 2021)

Introduction. Gamma Oscillations and Neuroplasticity

- Gamma power increase reflects synaptic changes consistent with Hebbian spike-timing-dependent plasticity (STDP)
- Repeated stimulation enhances the temporal precision of E-I interactions, tightening the gamma rhythm
- This selective process sharpens population coding by amplifying relevant inputs and suppressing weaker ones

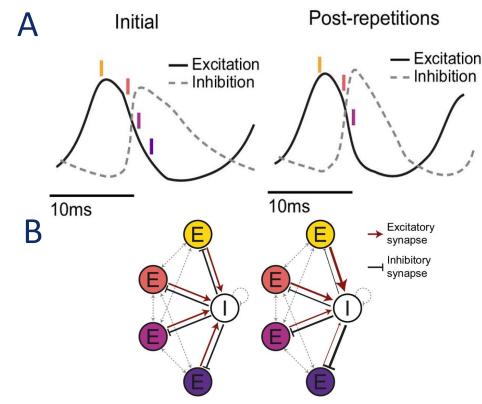


Figure 3. (A) Local average excitatory inputs (black solid curve) and inhibitory inputs (gray dashed curve). (B) Possible neural mechanism of changes in gamma activity, induced by repeating stimulation (Stauch et al., 2021)

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Research Aims and Objectives

Aims:

- Assess cortical E-I balance in VSS
- Evaluate repetition-dependent neuroplasticity in VSS

Objectives:

- Measure gamma-band oscillations in response to increasing excitatory drive
- Track single-trial gamma-power dynamics during prolonged visual stimulation
- Evaluate whether VSS patients show deviations from control group





Research Hypotheses

Hypotheses:

VSS participants will show altered average gamma power and frequency parameters as well as their modulation by drift rate, reflecting disrupted E-I balance

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patients will show maladaptive repetitiondependent plasticity compared to healthy controls that will be reflected in altered repetition-related gamma parameters



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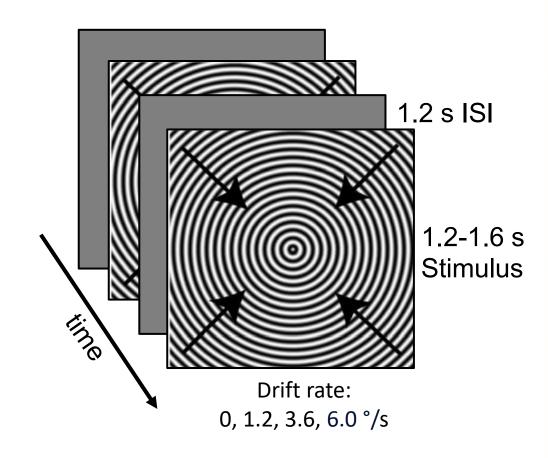
Methods. Participants & Stimuli

Participants:

26 VSS (26.7 +/- 5.6 years, 14 m.) and
 27 control (26.9 +/- 4.2 years, 16 m.) subjects

Experimental Paradigm:

- High-contrast annular gratings (18°, 1.66 cycles/°, 100%)
- 90 presentations of each of 5 drift rate conditions
- Button press in response to stimulus disappear



Methods. MEG Analysis

MEG raw data epoching (-1.0 to +1.6 s; baseline -200 to 0 ms)

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- Time-frequency analysis (400-1200 ms, 35-100 Hz, max power gradiometers)
- Average and single-trials GR power and frequency extraction
- ANOVA (averaged GR parameters) and LMM (single-trials GR parameters) statistical analysis

MEG Recording Preprocessing: MaxFilter, ICA, Epoching Time-Frequency Analysis Sensor Selection: Max GR **GR Power & Frequency Extraction** Statistics: ANOVA + LMM

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Results. Symptoms Severity

 Patients with VSS showed higher trait anxiety levels compared to healthy controls

 The visual discomfort scale revealed significant differences between groups

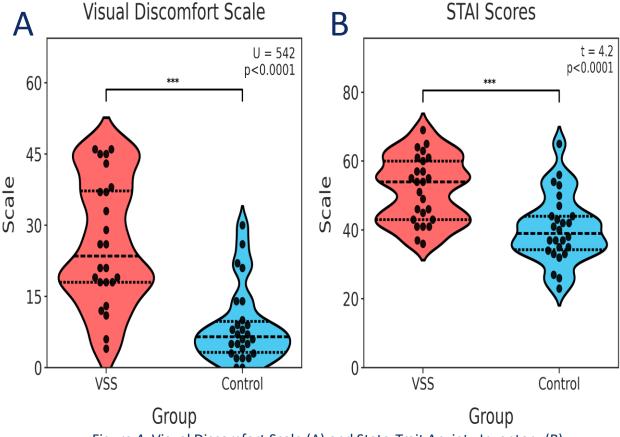


Figure 4. Visual Discomfort Scale (A) and State-Trait Anxiety Inventory (B) results for VSS and control groups

Results. Average GR Power

GR power shows inverted-U dependence on drift rate

• GR power peaks at intermediate drift rate $(F(4,204)=54.6, p<0.001, \eta p^2=0.52)$

No group differences in GR power

 Both groups showed similar GR power modulation (no significant effect of group or group*condition interaction)

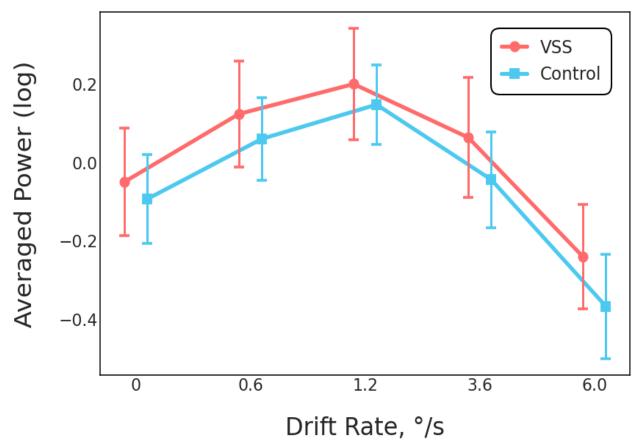


Figure 5. Changes in the log-transformed average GR power as a function of grating drift rate in patients with VSS and control participants

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Results. Average GR Frequency

Gamma frequency increased with drift rate

• Significant drift rate effect $(F(4,208)=327.3, p<0.001, \eta^2=0.86)$

No group differences found

 Both groups showed similar GR frequency modulation (no significant effect of group or group*condition interaction)

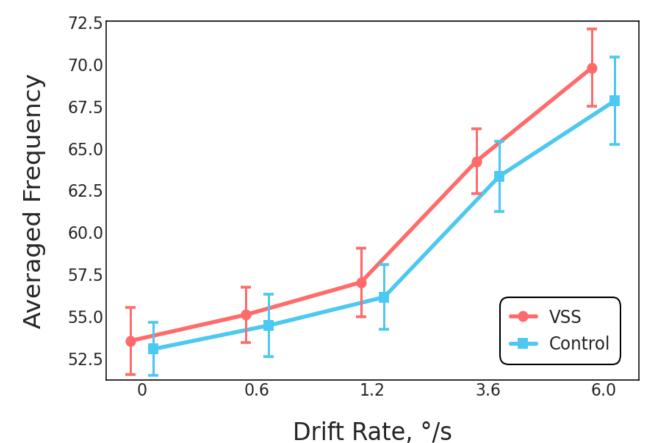


Figure 6. Changes in the average GR frequency as a function of grating drift rate in patients with VSS and control participants

Results. GR Power Block Analysis

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Power increased from Block $1 \rightarrow Block 3$ across all conditions

The rise in GR power over blocks indicates that stimulus repetition effects on neural activity are robust across different task conditions

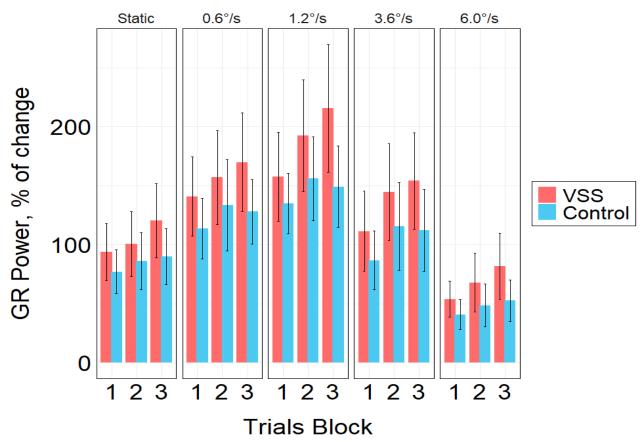


Figure 7. Median values of GR power in three blocks of trials (1: 15-55, 2: 56-96, 3: 97-137) plotted separately for experimental groups and drift rate conditions

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Results. GR Power Single-Trial Analysis

Biphasic pattern with stimulus repetition:

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early suppression → near linear increase

VSS participants showed a more pronounced increase in GR power:

GR_power ~ trialN*group + (1 + trialN | subject) + (1 + trialN | condition)

Significant trialN*group interaction (t(51.15) = 2.26, p = 0.028, d = 0.32)

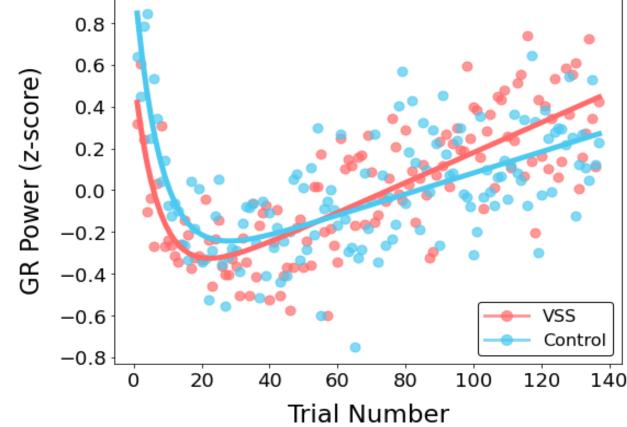


Figure 8. Time courses of z-transformed gamma response power in VSS and control groups

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Results. GR Power Regression Coefficient

Stronger repetition-related GR power increases in VSS participants

 No correlation between regression coefficient and Visual Discomfort scale scores in patients with VSS (r=0.02, p = 0.93)

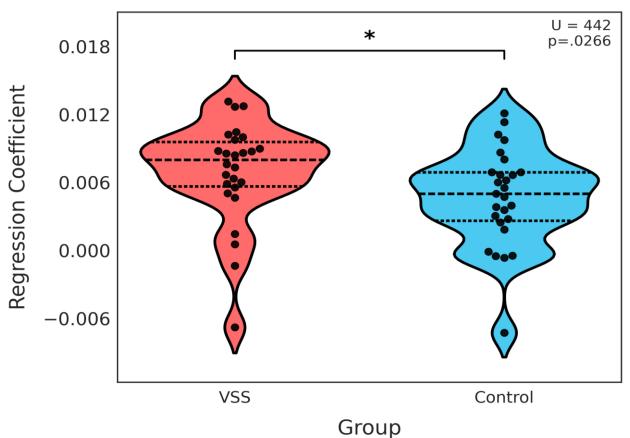


Figure 9. Individual regression coefficients for 15-137 trials averaged across drift rates in control and VSS groups

Conclusions

- 1. VSS patients show heightened visual cortex plasticity, with stronger gamma power increases during repeated stimulation, suggesting maladaptive neural adaptation.
- 2. No evidence of excitation-inhibition imbalance was found, indicating preserved local circuit function despite symptoms.
- 3. These findings highlight gamma oscillations as a potential biomarker and suggest targeting plasticity in future treatments.

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Results. Gamma Response Frequency

GR frequency does not differentiate between groups

GR_frequency ~ trialN * group +
(1 + trialN | subject) + (1 | condition)

- No significant group effect (t(50.0) = 0.52, p =0.60, Cohen's d = 0.06)
- No significant trialN and group interaction (t(48.6) = 1.21, p= 0.23, Cohen's d = 0.17)

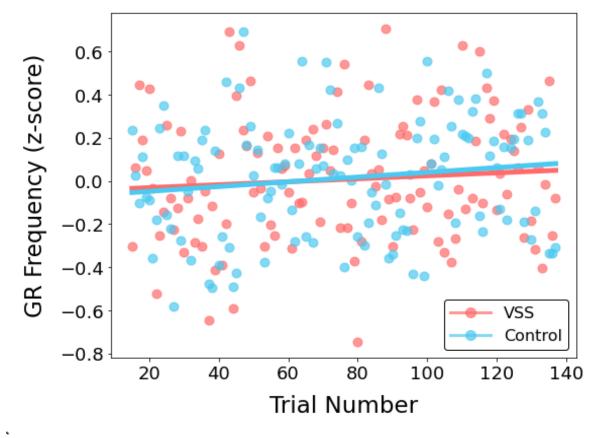


Figure 10. Time courses of z-transformed gamma response frequency in VSS and control groups

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Results. Behavioral Performance

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VSS subjects showed weaker inhibition:

- Comission Errors: U = 427.0, p = 0.0269
- Omission Errors: U = 278.5, p = 0.5110

Performance pattern was similar across groups:

- Significant effect of Condition on RT
- No Group effect or Group x Condition interaction

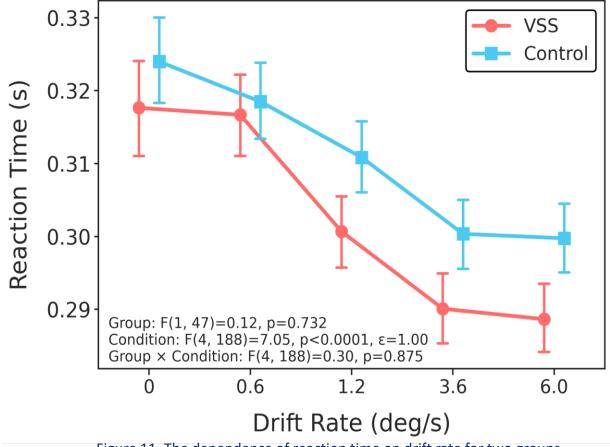


Figure 11. The dependence of reaction time on drift rate for two groups.

Mixed ANOVA analysis results for group, condition factors and their interaction are shown

Results. GR Grand Average Spectrum

- The high-frequency tail shape of gamma spectra did not differentiate between groups
- Absence of differences in grand average gamma spectra suggests preserved E/I balance in VSS and controls

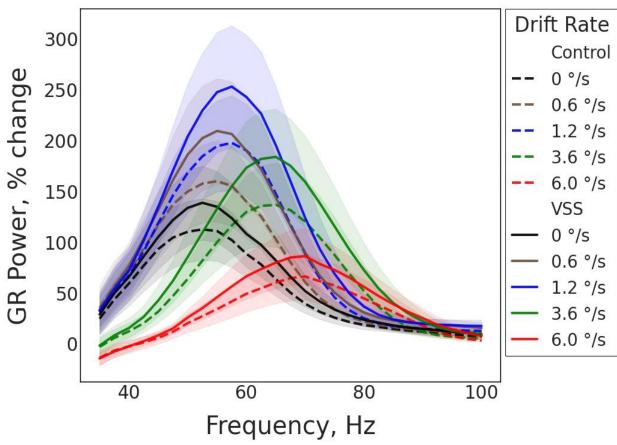


Figure 12. Grand average spectra of normalized GR. The spectra are shown for four motion velocity and two groups of subjects. Shaded areas represent 95% confidence intervals