Abstract #260 | Oral or Poster presentation

Transcranial Photoacoustic Imaging of NMDA-Evoked Focal Circuit Dynamics in Rat Hippocampus

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Introduction

Transcranial functional photoacoustic (fPA) voltage-sensitive dye (VSD) imaging promises to overcome current temporal and spatial limitations of current neuroimaging modalities. The technique previously distinguished global seizure activity from control neural activity in groups of rats. To validate the focal specificity of transcranial fPA with VSD (IR780 perchlorate) imaging *in vivo*, we now present proofs-of-concept that the results differentiate N-methyl-D-aspartate (NMDA) evoked neural activity in rat hippocampus. Concurrent quantitative EEG (qEEG) and microdialysis recorded real-time circuit dynamics and glutamate concentration change, respectively. We hypothesized that location-specific fPA VSD contrast would identify the neural dynamics in hippocampus with the correlation to NMDA evoked focal glutamate release and time-specific EEG signals.

Methods

To test the hypothesis, we infused 0.3, 1, and 3 mM NMDA at 2 µl/min over 60 min via an implanted microdialysis probe. The dialysate samples collected every 20 minutes during the infusion were analyzed for focal changes in extracellular glutamate release and quantified by high-performance liquid chromatography (HPLC).

Results

Transcranial fPA VSD imaging provided NMDA evoked VSD responses at the contralateral side of the microdialysis probe, presenting positive correlation with glutamate increase during 3 mM NMDA infusion. On the other hand, insignificant VSD response and glutamate release were obtained during 0.3 mM NMDA infusion. Quantitative EEG (qEEG) successfully confirmed induction of focal seizure activity or low response during 3 mM and 0.3 mM NMDA infusion, respectively. This graded response suggests all-or-none gating system in the dentate gyrus (DG) in hippocampus.

Conclusion

We conclude that transcranial fPA VSD imaging distinguished graded DG gatekeeping functions, based on the VSD redistribution mechanism sensitive to electrophysiologic membrane potential. The results suggest the potential future use of this emerging technology in clinics and science as an innovative and significant functional neuroimaging modality.

Acknowledgment

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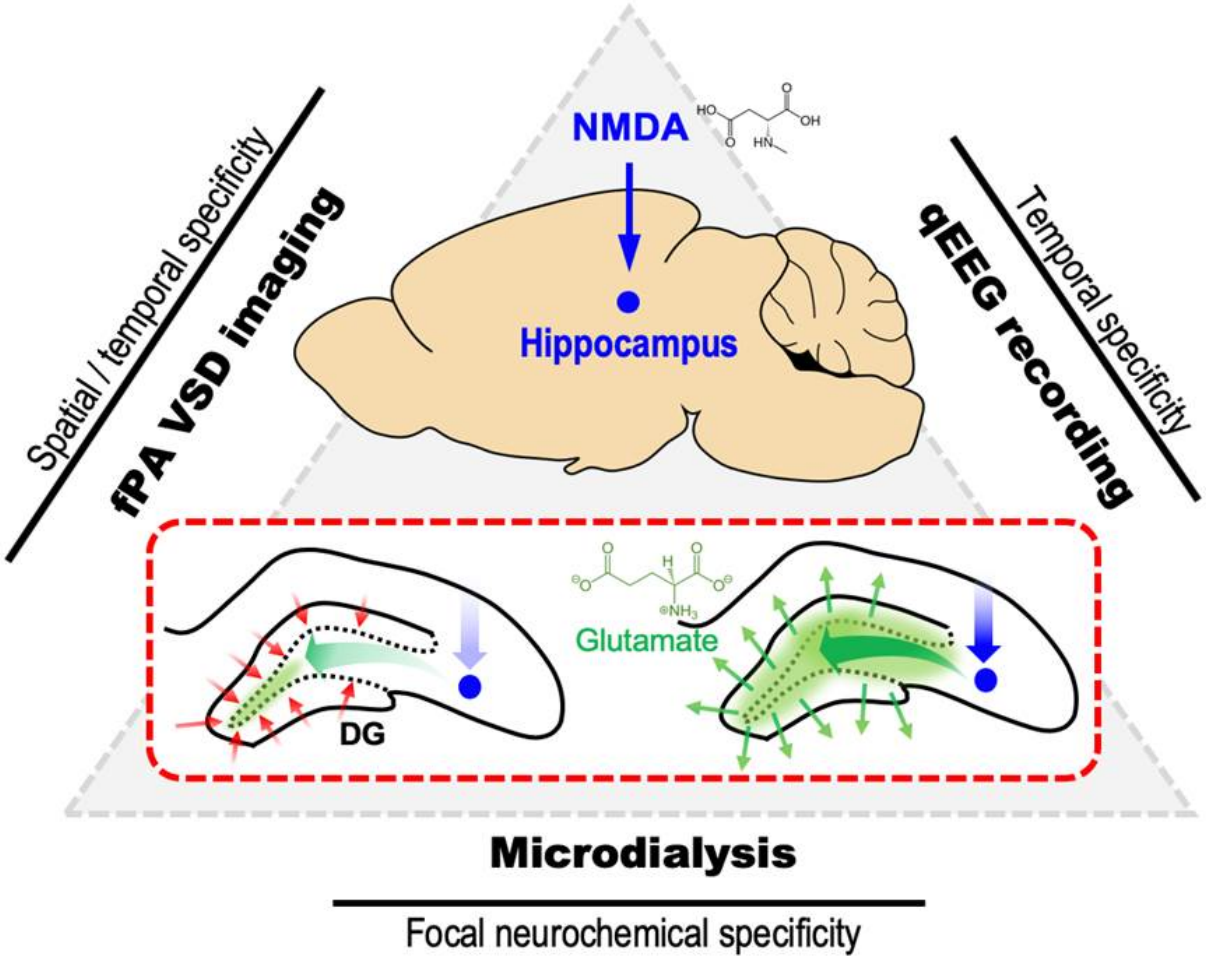
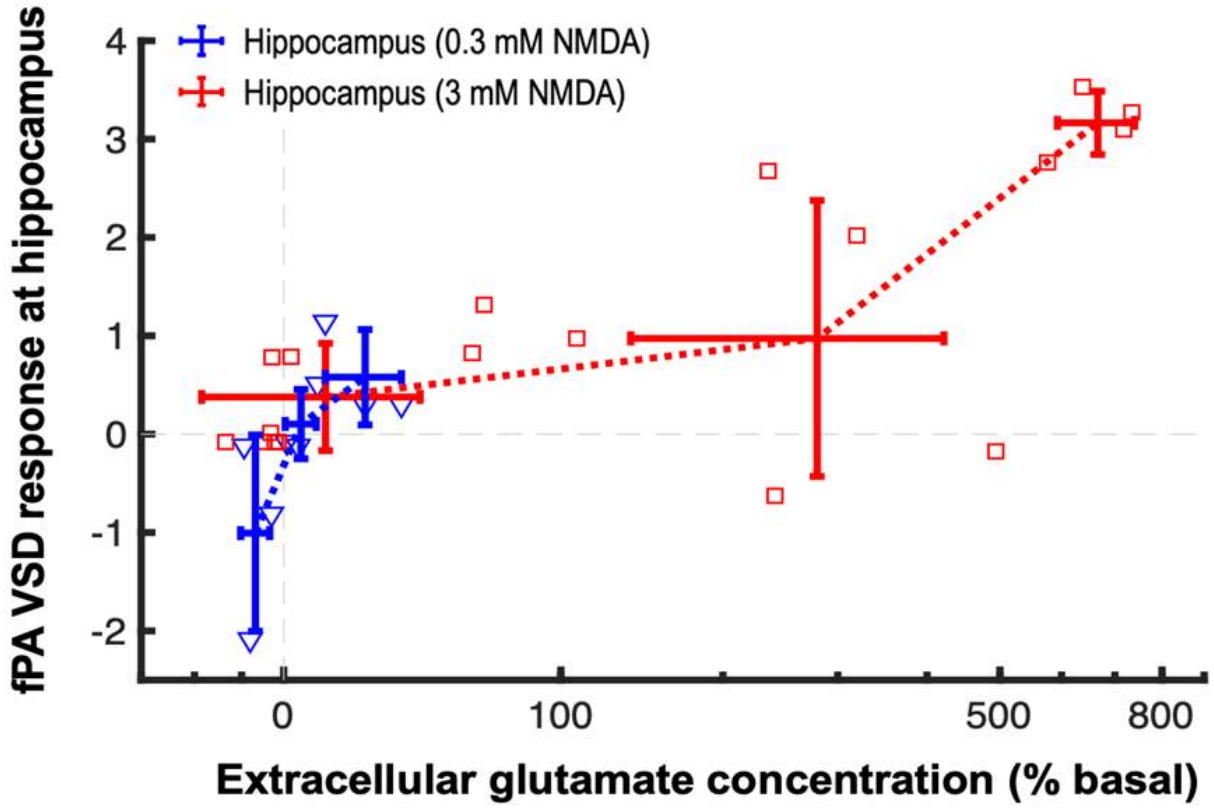


Trimodel Sensing of Distinct changes in Electrophysiology at Hippocampus
Red dotted rectangle describes breakdown of dentate gyrus (DG) gating at hippocampus in response to focal NMDA infusion. NMDA, N-methyl-d-aspartate; VSD, voltage sensitive dye (Kang Jeeun et al., Journal of Neural Engineering, in press).



Response of fPA VSD at Hippocampus
The figure shows the fPA VSD response at hippocampus as function of extracellular glutamate concentration. Grey dotted lines indicate the basal level in fPA VSD response and extracellular glutamate concentration (Kang Jeeun et al., Journal of Neural engineering in press).