

Study the role of GluN3A in psychiatric symptoms

Using suitable model systems, how would you propose to elucidate and validate the putative role of GluN3A in symptoms related to mental illness?

Answers to this <u>question</u> including a proposal for collaboration can only be considered if they arrive no later than April 29, 2025, 11:59 pm PST.



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What is the context of the problem that we would like to solve?

N-methyl-D-aspartate receptors (NMDARs) and other ionotropic glutamate receptors (iGluRs) mediate most of the excitatory signaling in the mammalian brains in response to the neurotransmitter glutamate. While NMDARs have been studied extensively over the past decades for their roles in neurotransmission and plasticity, the atypical subunit GluN3A (also known as NR3A, encoded by the human gene GRIN3A, Grin3a in rodents) of the NMDAR family was discovered only relatively recently. By assembling with GluN1, GluN3A forms excitatory cation channels which are activated exclusively by glycine, the neurotransmitter conventionally mediating inhibitory signaling when it binds to pentameric glycine receptors. The function of GluN3A containing receptors at the circuit and systems level remains largely unclear, though. The anatomical expression profile of GluN3A, including the ventral hippocampus, the medial habenula, the amygdala, the thalamus, and cortical somatostatinexpressing interneurons, suggests a potential involvement in brain processes relevant to psychiatry, including cognition and emotion. The lack of a selective pharmacological modulator of sufficient quality to be used for in vivo experiments has hampered progress in our understanding at the systems level. While the behavior of knockout mice, both constitutive and conditional, does support the hypothesis of GluN3A's involvement in both cognition and negative valence, a lot remains to be learned about the wider role of GluN3A in emotion and behavior.

So, to summarize, as part of this call, we are looking for solutions which are likely to increase our understanding of GluN3A's impact on physiology and behaviors that are related to symptoms of mental illness.

What potential solutions could be in scope?

- A strong scientific proposal with a new and compelling scientific idea to investigate GluN3A's impact on psychiatric symptoms, for example by:
 - Modulation of GluN3A using genetic tools like siRNA or CRISPR/Cas9
 - Measurement of behavioral and/or physiological readouts with a strong link to psychiatric symptoms
- Initial data are a plus, but conceptual proposals are acceptable

What potential solutions would be out of scope?

- Proposals that exclusively focus on molecular or cellular mechanisms without providing a link to behavior or macrocircuit function
- Purely computational approaches
- Human genetic studies
- Proposals focusing on mechanisms of action that are unique to non-human species



- In vitro assays to address activity of any modalities modulating GluN3A activity
- Solutions narrowly focused on cognitive symptoms of schizophrenia
- Contract research service proposals for modulation of GluN3A

What benefits do we offer to you in exchange for having submitted a solution?

If your project is selected, you will have the opportunity to directly collaborate with the Neuroscience & Mental Health Discovery Research team of Boehringer Ingelheim.

As an incentive specific to this opn2EXPERTS call, we offer an exclusive access to advanced small molecule tool compounds ready for *in vitro* and *ex vivo* testing to validate your submitted hypothesis, should your proposal be selected by our scientific review team. In addition, you can also expect appropriate funding for the prospective collaboration period. Your exact funding request should be outlined in your proposal. As a framework, we suggest that your initial funding request is structured in milestones and does not exceed 250,000 euros per submitted project in total (including direct, indirect, and overhead costs).

The opportunity for a funded stay at Boehringer Ingelheim for technology exchange / training is potentially available, as is the availability of custom biological tools and reagents.

Our collaboration agreement will provide full transparency about each partner's rights & obligations (including intellectual property rights). As part of the agreement, you will be encouraged to publish following the collaboration agreement (to be negotiated in good faith).

What are the key success criteria on which we base our selection for the best answer?

We are seeking research collaboration proposals that contain:

- A well-structured proposal outlining a new and compelling scientific approach including an experimental plan that will be used to test your hypothesis.
- Outlining of the technical feasibility, and potentially existing data or previous publications that support feasibility / experience with outlined technology, based on existing techniques and established assays.
- Your exact funding request should be outlined in your proposal based on a well-thoughtthrough project. The project should be structured in milestones and planned with key decision points (clear Go/No-Go criteria). The funding request for the initial milestones resulting in a Go/No-Go decision should not exceed 250,000 euros per submitted project in total and must cover both direct and indirect costs.
- Proven track record in the required field of expertise.
- Ability to implement the outlined solution as part of a scientific collaboration project with Boehringer Ingelheim including access to a laboratory.



What information should be included in your answer submission?

Please use our answer submission template to provide a 2-3 page <u>non-confidential</u> proposal (available for download on the following <u>site</u>).

If confidential data exists that would strengthen the proposal, please indicate that information is available to share under a Confidential Disclosure Agreement (CDA). If we find the nonconfidential concept proposal sufficiently interesting, we will execute a CDA for confidential discussions.

Anticipated Project Phases or Project Plan

Phase 1	Please complete your submission by April 29, 2025, 11:59 pm PST at the very latest.
Phase 2	Our review of all proposals will be completed by mid-June 2025 and scientists will be informed after that.
Phase 3	Start of discussions for the collaboration agreement in Q3-4/2025.

Submitting a collaboration proposal

- Check the outline of the opn2EXPERTS "<u>Study the role of GluN3A in psychiatric symptoms</u>" on opnMe.
- Alternatively, you may click the "Get Submission Template" banner to access the material transfer template.
- Follow the instructions to upload your submission document (requires login or registration).
- The upload allows you to attach additional application files if desired.
- You will be able to access your final submitted collaboration proposal in your personal dashboard and follow its review status.
- Please also visit the <u>FAQ section</u> on opnMe.com to learn more about our opn2EXPERTS program.

