A New Dawn for Social Anxiety Treatment

Clinical Advancement of the Novel V1a Receptor Antagonist, NTX-1472

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Social Anxiety Disorder

Disease Background

- Intense fear or anxiety about social situations and concern about negative evaluation of others
- Age of onset typically in adolescents and young adults
- Results in social, education and occupational impairment
- Subtype: performance-only

Unmet Need

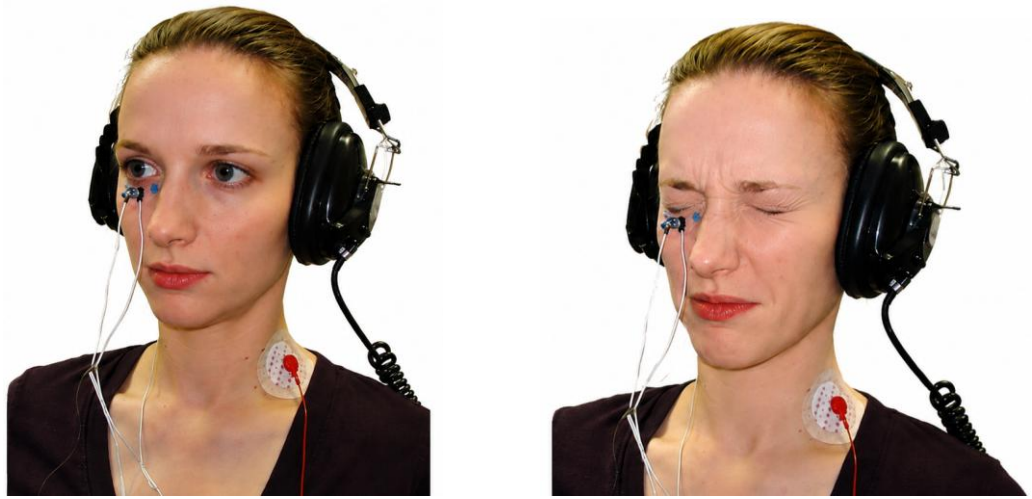
- Lifetime prevalence of 6-13%
- Current treatments monoaminergic, require 4-6 weeks to have a significant impact, high discontinuation rates
- 50% patients do not achieve remission (lowest rate of all anxiety disorders)
- **No approved pharmacological treatments that directly target social-threat processing**

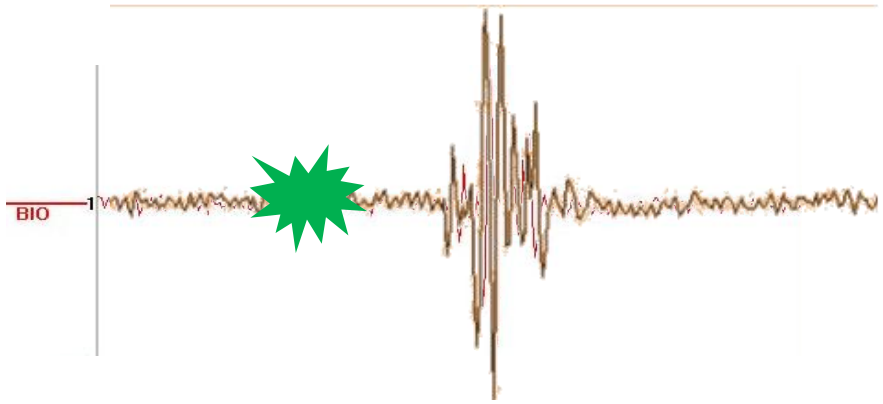
20 million

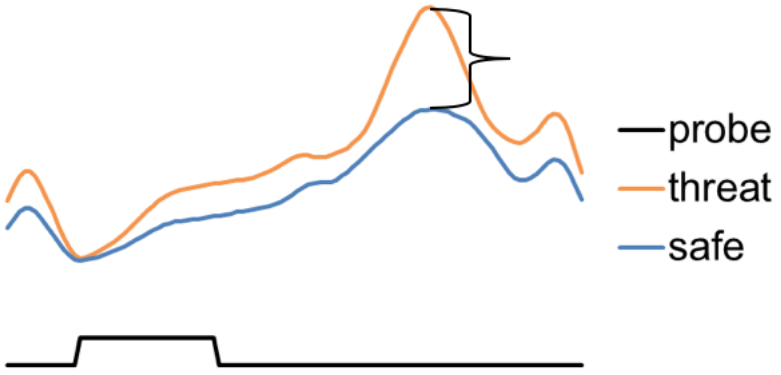
Adults suffer with social anxiety disorder (US)

Anxiety & Depression Association of America; Stein & Taylor 2025; Tremmel et al. 2025

Translational Measure of Negative Valence: Startle Response

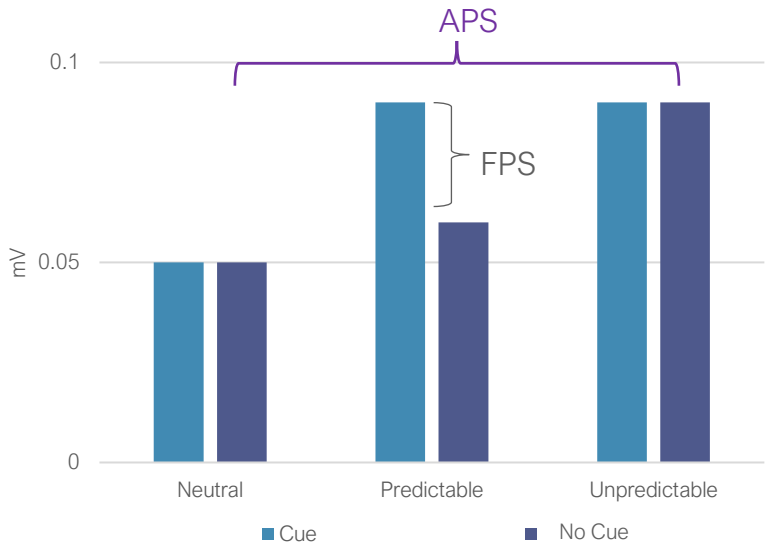






Anxiety-Potentiated Startle: Physiological Biomarker for Anxiety Disorders & Treatment Development

National Institute of Mental Health



- NPU (Neutral-Predictable-Unpredictable) Paradigm separates neurophysiological responses to:
  - Unpredictable threat (anxiety-potentiated startle; APS)
  - Predictable threat (fear-potentiated startle; FPS)
- APS but not FPS attenuated by pharmacological anxiolytics (SSRIs, benzodiazepines) and behavioral interventions (moderate exercise) in **healthy adults**


ELSEVIER
Biological Psychiatry
Volume 95, Issue 1, 1 January 2024, Pages 85-92

Archival Report

Attenuation of Anxiety-Potentiated Startle After Treatment With Escitalopram or Mindfulness Meditation in Anxiety Disorders

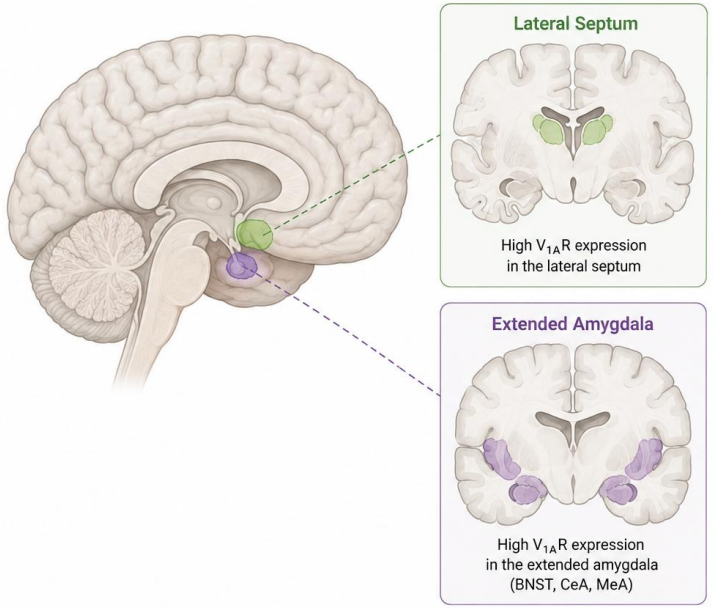
Elizabeth A. Hoge [a], Caroline H. Armstrong [c], Mihriye Mete [b], Isabelle Oliva [c], Sara W. Lazar [c], Tiffany R. Lago [d], Christian Grillon [e]

- Double-blind, placebo-controlled, parallel-arm design
- APS higher at baseline in **adults with anxiety disorders** (n=93) than healthy controls (n=66)
- APS normalized after 8 weeks of treatment with both Escitalopram and Mindfulness Based Stress Reduction (MBSR)

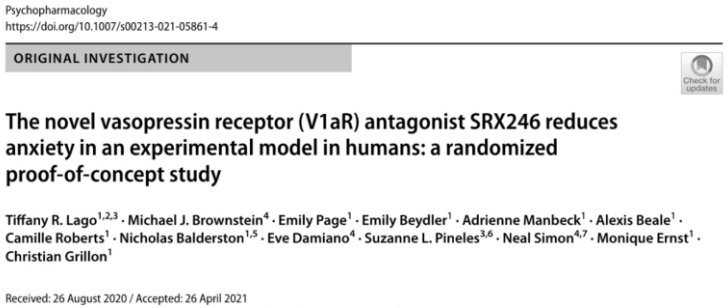
Grillon et al 2006, 2008, 2009, 2015; Gorka et al 2013; Hoge et al 2024; Lago et al 2018; Nelson et al 2013

V1aR Antagonism Decreases Anxiety-Potentiated Startle in Humans

National Institute of Mental Health



- Arginine vasopressin (AVP) is an affiliative neuropeptide, closely related to oxytocin (OT)
- AVP-OT system critical to regulation of social behavior and stress responses
- AVP enhances response to threat and negative emotional stimuli
- V1a receptor (V1aR) is G protein-coupled receptor highly expressed in lateral septum and extended amygdala
- V1aR expression related to social recognition and anxiety behavior in preclinical models



Psychopharmacology
https://doi.org/10.1007/s00213-021-05861-4

ORIGINAL INVESTIGATION

The novel vasopressin receptor (V1aR) antagonist SRX246 reduces anxiety in an experimental model in humans: a randomized proof-of-concept study

Tiffany R. Lago[1,2,3] · Michael J. Brownstein[4] · Emily Page[1] · Emily Beydler[1] · Adrienne Manbeck[1] · Alexis Beale[1] · Camille Roberts[1] · Nicholas Balderston[1,5] · Eve Damiano[4] · Suzanne L. Pineles[3,6] · Neal Simon[4,7] · Monique Ernst[1] · Christian Grillon[1]

Received: 26 August 2020 / Accepted: 26 April 2021

- Phase 2, double-blind, placebo-controlled, cross-over study
- Healthy adults (n=36)
- **V1a antagonist decreased APS** compared to placebo, regardless of drug order

Bredewold & Veenema 2018; Lago et al 2021; Mavrych et al 2025; Zhang et al 2026

NTX-1472: From Mechanism to Optimized Therapeutic Candidate

V1aR Pipeline

- Leveraged findings from predecessor **balovaptan** program supporting improved socialization in adult males with autism

Preclinical Program

- K_i of 0.5 ± 0.04 nM
- At least 6000-fold binding selectivity for V1aR
- Toxicology and safety assessments (rats, cynomolgus monkeys) support up to 12-week dosing

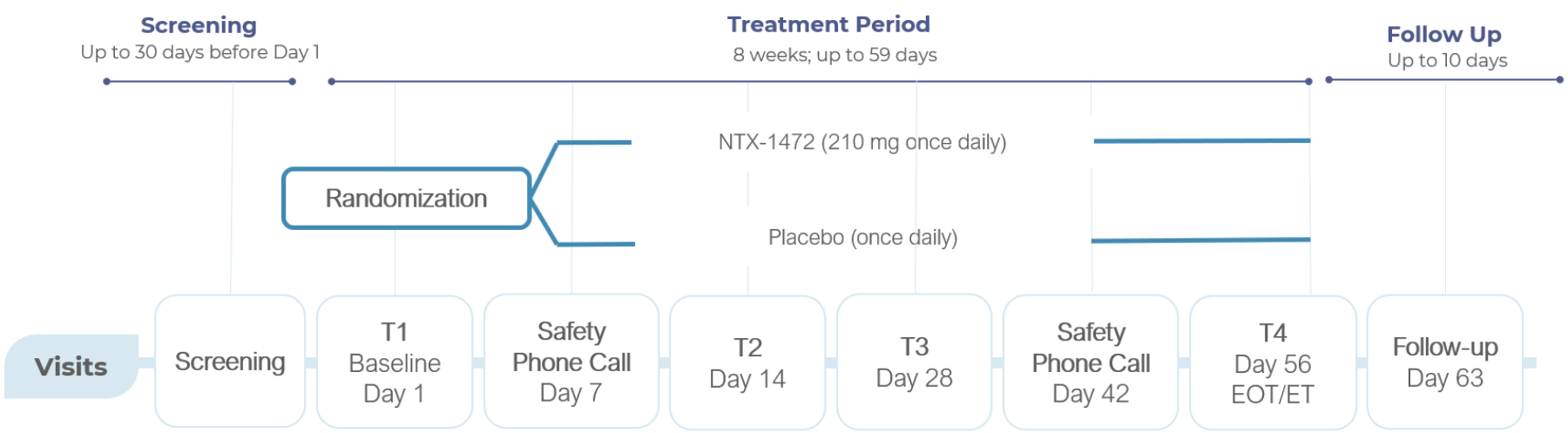
Phase 1 Clinical Program

- Completed SAD (up to 360mg), MAD (up to 210mg), and drug-drug-interaction (n=104)
- Generally safe and well-tolerated
- No drug-related SAEs
- PK properties and modeling support once daily administration

Poster W10

Bolognani et al 2019; NTX-1472 IB

Phase 2 Program: Proof-of-Concept Study in Social Anxiety Disorder (SOAR)



NCT07323784

Thank you to our investigators, collaborators and participants!

Sample: N=100 (50 participants per arm, stratified by sex)

Primary Endpoint: Incidence & Severity of TEAEs
Secondary Endpoints: LSAS, CGI, HAM-A, UCLA-LS-10, DASS-21 stress

Topline Data Expected 1H2027

Liebowitz Social Anxiety Scale; Clinical Global Impression, Hamilton Anxiety Rating Scale; UCLA Loneliness Scale; Depression Anxiety Stress Scale

Conclusion

Key Takeaways

- V1aR is a promising treatment target for Social Anxiety Disorder, as evidenced by translational and clinical findings that support modulating in social-threat processing.
- SOAR study to provide foundational data for later-stage clinical development of NTX-1472