

Guanfacine, an old drug with new tricks? Anxiolysis in lung transplant.

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Background

- Anxiety is common in the post lung-transplant period¹⁻² for reasons including:
 - shortness of breath, pain
 - Med SE (tacrolimus, steroids)
 - psychological factors
 - invasive surgery, prolonged hospitalization, lifestyle changes
- Severe anxiety interferes with recovery:
 - Prolonged vent weaning
 - Need for additional sedation → Delirium
 - Decreased PT/OT engagement
- Treatment is limited by need to balance risk for delirium, respiratory depression, and drug interactions³
- Guanfacine, a potent centrally-acting alpha-2 agonist, may provide a safe and effective alternative in the acute hospital setting.

Guanfacine

Pharmacologic properties:

- Central alpha-2 receptor agonist → sympathetic tone reduction⁴
- Immediate release (*Tenex*): T_{1/2} = 17 hours; T_{max} = 1-4 hours⁵
- Extended release (*Intuniv*): T_{1/2} = 14-18 hours; T_{max} = 5-8 hours⁵

Safety and tolerability:

- Less delirigenic than alternative sedatives⁶
- May reduce use of more sedating/deliriogenic/respiratory depressant medications (e.g. benzodiazepines)⁶
- Adverse effects: hypotension, bradycardia; sedation (extended release)^{4,7,8}
- Overall, well tolerated. Cardiovascular effects tend to be transient (during uptitration), statistically mild-moderate, and clinically tolerated.⁷⁻⁹
- Possible interaction with common immunosuppressives:⁴
 - Cyclosporine, tacrolimus, prednisone, azathioprine, may increase serum level of guanfacine
 - Guanfacine may increase levels of mycophenolate

Anxiolytic properties:

- Though there have been mixed results, studies have shown decreased anxiety and/or improved affect after alpha-2 agonist [clonidine].¹⁰
- Animal studies:
 - Guanfacine decreased anxiety behaviors during cocaine withdrawal (rats)¹¹
 - Guanfacine attenuates the harmful effects of stress on the brain by interrupting cell signaling that leads to neuronal atrophy (rats)¹² (mice)¹³
 - Guanfacine may have analgesic effects on visceral pain (mice)¹⁴
- Human studies/reports:
 - Guanfacine did not show efficacy for treatment of pediatric chronic/primary anxiety disorders.⁹
 - Srour et al described the successful use of guanfacine for controlling severe anxiety and agitation (not related to delirium) while weaning mechanical ventilation after cardiac surgery.¹⁵

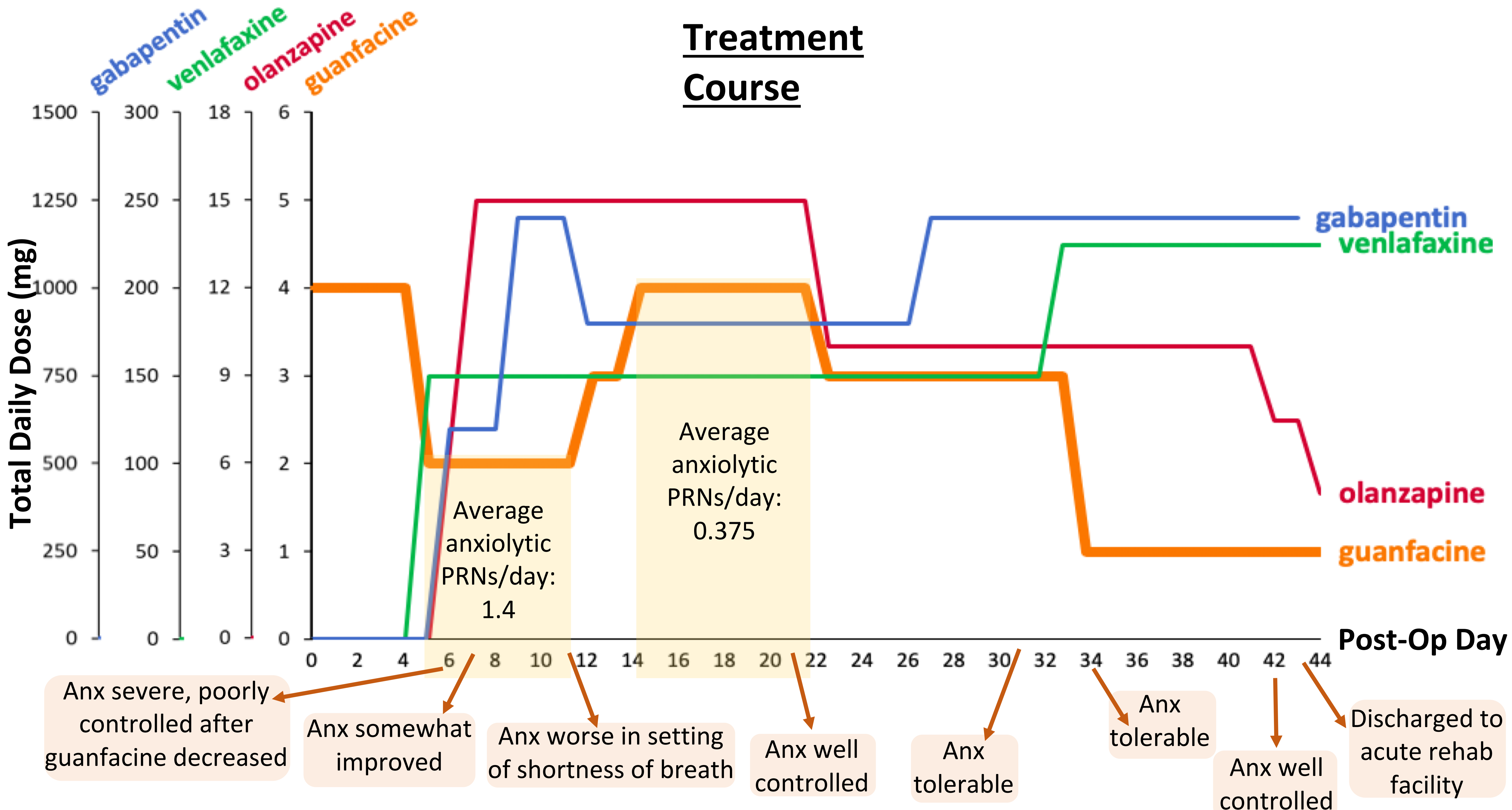
Discussion and Conclusions

Guanfacine has been studied in humans for treatment of chronic psychiatric disorders, but scant data is available for acute anxiety in a hospitalized adult population. There is a theoretical role for alpha-2 agonism to have anxiolytic effects, and animal models suggest there may be analgesic effects as well. These effects could be useful in augmenting anxiety management in the post lung-transplant period.

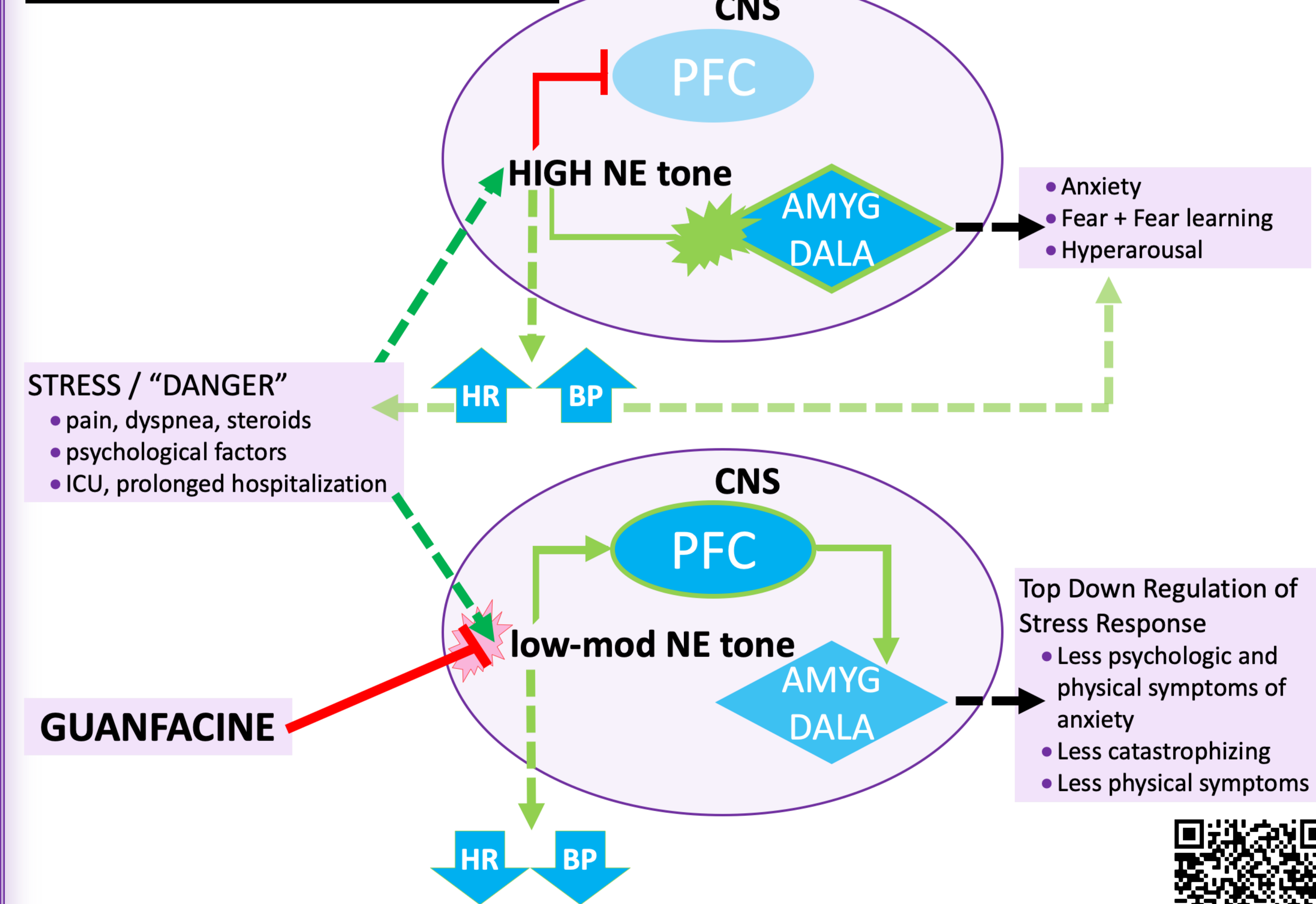
The treatment of acute anxiety in the hospitalized patient status post lung transplant is extremely limited. Guanfacine may be an under-studied and under-utilized tool for acute anxiolysis that has a quick-onset, is short-acting and safe, has relatively low risk of dangerous drug-drug interactions, and does not cause respiratory depression.

We invite colleagues to consider furthering evidence with empiric study and formal consideration of this seasoned medication with this new clinical application.

Case 48yo patient with history of hypothyroidism, obesity, depression and anxiety, admitted for severe COVID infection requiring lung transplant. Guanfacine was started by the primary team as a bridge off dexmedetomidine sedation. Psychiatry was consulted 5 days post transplant due to refractory anxiety in the setting of perceived dyspnea.



Theoretical Mechanism¹⁶⁻¹⁹



References: