An Open-Label Study of Low-Dose Ketamine Shows Correlation Between Reduced Sensory Symptoms and Improved Behavioral Symptoms in Children with ADNP Syndrome


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METHODS

Hypothesis:

• Activity dependent neuroprotective protein (ADNP) syndrome is a genetic neurodevelopmental disorder characterized by sensory reactivity, cognitive delays, autism features, and behavioral problems1.
• Ketamine, an NMDA receptor antagonist, may upregulate the ADNP gene, suggesting it might compensate for ADNP haploinsufficiency2,3.
• Our group previously reported nominal improvements in social behavior, hyperactivity, repetitive behaviors, and sensory sensitivities in a pilot open-label clinical trial in ADNP syndrome using a single infusion of low-dose ketamine (0.5mg/kg)4.

Participants

• Improvements in sensory symptoms would correlate with ADNP syndrome using a single infusion of low sensory sensitivities in a pilot open

Social behavior, hyperactivity, repetitive behaviors, and behavioral problems characterized by sensory reactivity, cognitive delays, autism

Activity dependent neuroprotective protein (ADNP)

RESULTS

Bivariate Pearson correlations were calculated based on results demonstrated greatest change.

Figure 1. Schematic representation of study design.

Clinical Assessments

• A series of caregiver questionnaires were used to monitor behavioral outcomes of treatment:
  • Sensory Profile (SP) was used to evaluate sensory processing; higher scores reflect fewer sensory symptoms.
  • Aberrant Behavior Checklist (ABC) was used to measure problem behaviors; lower scores reflect fewer behavioral symptoms.
  • Bivariate Pearson correlations were calculated based on percent change, from Baseline to Week 1.

OBJECTIVE:

• Here, we aimed to investigate whether improvements seen in sensory and behavioral symptoms correlated.

Hypothesis:

• We hypothesized that after receiving ketamine, children’s improvements in sensory symptoms would correlate with improvements in behavioral symptoms.

Future Directions:

• We found moderate correlations between improvement in behavioral symptoms and both sensory seeking and hyporeactivity (i.e., low registration).
• Sensory hyperreactivity scales were not related to behavioral change.
• This work indicates that change in low-level sensory features relate to higher order problem behaviors, suggesting that intervention on a sensory level might impact behavior.
• As sensory seeking behaviors, as well as irritability, hyperactivity, and social withdrawal, are all features of autism broadly, this work suggests that ketamine might impact both sensory functioning and behavior in autism as well.

FUNDING SOURCES

To read more about the ketamine in ADNP clinical trial, please scan here:

REFERENCES


CONCLUSIONS

• Reduction in SP Sensation Seeking significantly correlated with improvement in ABC Irritability (r=.69, p=.026) and Hyperactivity (r=.66, p=.037).
• Improvement in SP Low Registration significantly correlated with reduced ABC Social Withdrawal (r=.65, p=.026).
• Sensation Avoidance and Sensory Sensitivity scores improved with treatment over the one-week period but did not correspond to change in problem behaviors.

Figure 2. Average scores and standard errors of the mean of the Aberrant Behavior Checklist (ABC; A) and Sensory Profile (SP; B) at Baseline, Day 1 (ABC only), Week 1, Week 2, and Week 4, showing greatest improvement in both behavior and sensory symptoms from Baseline to one week following ketamine infusion. A. Results were significant for each subscale at Week 1, Week 2, and Week 4 (p<.05). B. Results were significant at Week 1 for Sensation Seeking, Sensation Avoidance, and Sensory Sensitivity; at Week 2 for Sensation Avoiding; at Week 4 for Sensation Avoidance and Sensory Sensitivity (p<.05).

Figure 3. Relationships between changes in sensory symptoms and change in behavioral problems.

• We will consider this intervention for other disorders with high levels of sensory seeking behaviors, such as autism.
• Future studies will also aim to explore whether neural processing of sensory information relates to these observed behavioral changes.

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Figure 3. Relationships between changes in sensory symptoms and change in behavioral problems.

• We will recruit more children with ADNP syndrome in order to evaluate whether these correlations hold with a larger sample size and to gain greater statistical power.
• We will consider this intervention for other disorders with high levels of sensory seeking behaviors, such as autism.
• Future studies will also aim to explore whether neural processing of sensory information relates to these observed behavioral changes.