

Seven Cases of Pediatric Acute-Onset Neuropsychiatric Syndrome with Celiac or Eosinophilic Esophagitis: Autoimmune Interplay and the Gut-Brain Axis

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BACKGROUND

- **PANS/PANDAS:** Immune-mediated, post infectious neuropsychiatric disorder (often Group A Strep) → **autoimmune inflammation in the basal ganglia associated with abrupt onset neuropsychiatric symptoms**
- **Celiac disease (CD):** Autoimmune enteropathy triggered by gluten, associated with malabsorption and neuropsychiatric manifestations²
- **Eosinophilic esophagitis (EoE):** Antigen-driven esophageal inflammation characterized by eosinophil-predominant infiltration³
- **Autoimmune comorbidities:** PANS/PANDAS patients frequently exhibit coexisting autoimmune diseases, suggesting broader systemic immune dysregulation⁴
- **Gap:** Prior reports suggest mixed but clinically meaningful overlap, yet real-world characterization of patients with both PANS/PANDAS and GI autoimmune or allergic disease is limited⁵

AIM

- Identify and characterize patients with PANS/PANDAS who also have concurrent Celiac Disease or Eosinophilic Esophagitis

METHODS

- Retrospective case series of 6 patients with PANS/PANDAS and concurrent CD/EoE evaluated at the DHMC NIPD Clinic (2019-2024)

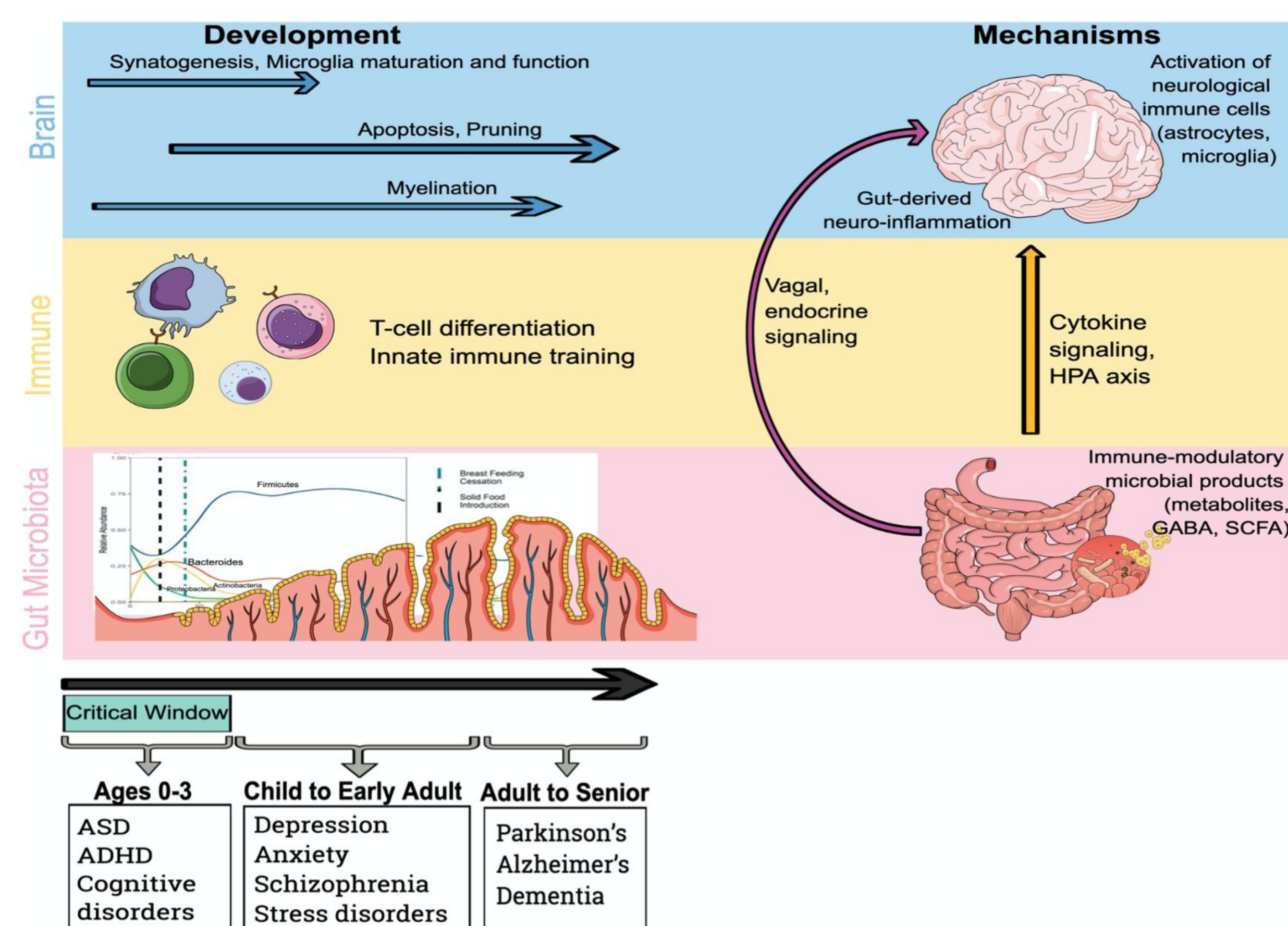


Figure 1: Developmental and mechanistic overview of the gut-brain-immune axis linking dysbiosis to neuroinflammation and neuropsychiatric disorders

RESULTS

Case	Sex	Prior Psychiatric Dx Initial PANS Presentation	Age at Diagnosis of Celiac/EoE	Age at Diagnosis of PANS and Assoc. Infection	Celiac/EoE symptoms correlate with psychiatric flares?	PANS Treatment Psychiatric treatments (Psy) Immunomodulation (IM) Antibiotics (Ab)
CD1	M	OCD, panic attacks, depression, challenges sleeping and toileting, tics, hand washing induced excoriated rash, auditory hallucinations	12 (elevated TTG found with PANS testing)	12 Group A Strep	Unclear	Psy: Sertraline, CBT/ERPT IM: NSAIDs, Rituximab, IVIG, Steroids
CD2	M	Prior dx: ASD level 1, ADHD OCD, behavioral dysregulation, tics, anxiety	8	11 Group A Strep	Gluten contamination associated with changes in mood Flares associated with GI upset	Psy: Abilify, Qelbree, CBT/PMT IM: Steroid bursts, Hydroxychloroquine Ab: Azithromycin
CD3	F	Prior dx: Anxiety related to food/gluten Severe anxiety, challenges sleeping, emotional dysregulation, ARFID, academic decline	8	9 Mycoplasma Pneumoniae	Unclear	Psy: Sertraline, Hydroxyzine, CBT IM: NSAID Ab: Azithromycin
CD4	M	Prior dx: ASD, MDD, mild GAD OCD, violence/aggression, challenges toileting, abrupt eating restriction, severe anxiety	5	7 Infectious trigger unknown	Unclear	Psy: Abilify, Sertraline, Ritalin, Family Therapy IM: Steroid burst, Ibuprofen Ab: Azithromycin
CD5	M	Prior dx: FPIES OCD, disruptive behavior, new onset tics, inattention/hyperactivity, behavioral dysregulation	2	4 Group A Strep	Parents identify gluten and FPIES as trigger for PANS flares	Psy: CBT IM: NSAIDs Ab: Azithromycin
CD6	F	OCD (germs), separation anxiety, tics, sensory sensitivities, urinary frequency	9	10 Group A Strep	GI sx related to anxiety	Psy: Sertraline, CBT/ERPT IM: NSAIDs Ab: Azithromycin
EoE1	M	OCD, acute onset separation anxiety, behavioral dysregulation, changes in appetite and aggression	5 Tx: Mometasone	Currently under evaluation for official PANS dx Onset age 6 - 3 weeks post URI	Parents identify EoE symptoms correlate with flares and NSAID usage for EoE improves flares	Psy: PMT IM: NSAIDs

DISCUSSION

- GI derived systemic immune signaling dysregulation is a potential driver underlying autoimmune overlap in PANS
- **Gut-brain immune axis:** Dysbiosis and antigen exposure increase gut permeability and cytokine → neuroinflammation^{6,7,8}
- **Leaky gut framework:** Zonulin-mediated permeability in Celiac and eosinophil-driven epithelial injury in EoE may amplify systemic inflammation^{9,10}
- 7/7 patients had CD or EoE diagnosis before or coinciding with PANS onset → possible **immune priming** via chronic gut inflammation
- **Clinical correlation:** some families observed GI inflammation coinciding with PANS flares and psychiatric improvement with gluten-free or EoE-directed therapy¹¹

CONCLUSIONS

- Co-occurrence of CD and EoE in PANS patients may suggest an immune-mediated connection between the gut and brain
- Next steps include prospective studies assessing:
 - Microbiome composition
 - Biomarkers of gut permeability and inflammation (zonulin, calprotectin)
 - Longitudinal outcomes of GI-directed interventions on psychiatric symptoms.

