Holistic Clinical Integration in Presentations of PANS/PANDAS: A Narrative Review of Microbiome Shifts, HPA Axis Dysregulation, and Chiropractic Care

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Study Objective
To investigate the relationship between pediatric acute-onset neuropsychiatric syndrome (PANS/PANDAS) and gut microbiota ecology, and to assess gut microbial composition to gain further physiological information regarding the gut-brain axis in this disorder.

Study Design
Observational case-control study utilizing 16S rRNA-based targeted metagenomics.

Study Participants
Thirty PANS/PANDAS patients (aged 4 to 16 years, average age 10.03) were recruited and compared to 70 age-matched healthy controls. Inclusion criteria required the absence of active inflammatory, infective, or chronic diseases at the time of testing. Furthermore, all antibiotic and probiotic intake was suspended for two to four months prior to the evaluation.

Study Parameters Assessed
Researchers extracted genomic DNA from stool samples collected on consecutive days to identify and classify the bacterial species present, grouping closely related organisms into standardized taxonomic categories (operational taxonomic units, or OTUs). They then assessed the overall variety and richness of gut bacteria, both within each group and between the PANS/PANDAS and control groups (alpha- and beta-diversity), alongside computational estimates of the community's likely metabolic activity based on which bacteria were present rather than direct measurement (PICRUSt-predicted functional pathways). Finally, statistical correlation testing examined the relationship between specific bacterial genera and a blood marker of recent streptococcal exposure (anti-streptolysin O titer, ASLOT; Pearson correlation).

Primary Outcome Measures
As an observational case-control study rather than a controlled trial, there was no single prespecified primary outcome measure. The principal comparisons were: the overall diversity and density of gut bacteria within and between the two groups (alpha- and beta-diversity); which specific bacterial types were more or less abundant in PANS/PANDAS patients versus controls (taxonomic composition); estimated differences in the gut community's likely metabolic activity, based on which bacteria were present rather than direct measurement (PICRUSt-predicted KEGG pathways); and the relationship between specific bacterial genera and a blood marker of recent strep exposure (anti-streptolysin O titer, ASLOT).

Key Findings
The PANS/PANDAS cohort showed a measurably narrower range of gut bacteria compared to healthy controls (lower alpha-diversity), indicating fewer distinct microbial species overall. Ecological analysis revealed two distinct age-related clusters, leading researchers to focus heavily on the younger 4-8 year cohort (y-PAN). This younger demographic exhibited a stark disequilibrium: an overgrowth of the Bacteroidetes phylum (including the genera Bacteroides and Odoribacter) alongside a reduction in beneficial Firmicutes. Computational estimates of the community's metabolic activity pointed toward an increase in inflammation-associated pathways and a decrease in pathways relevant to brain and nervous system function – specifically those involved in D-alanine, tyrosine, and dopamine metabolism. Furthermore, higher levels of a blood marker for recent streptococcal exposure (anti-streptolysin O titer, ASLOT, values greater than 500 units) were positively correlated with the presence of Odoribacter.

Practice Implications and Discussion
In the ever-evolving landscape of pediatric neuro-immune conditions, significant dialogue has turned to the impact of the gut-brain axis on presentations such as PANS and

PANDAS. The findings of this observational study highlight a critical intersection between gut dysbiosis, systemic immunity, and neurological function.

The original authors' finding of Firmicutes depletion in the younger PANS/PANDAS cohort carries more clinical weight than a simple microbiome shift. Firmicutes are the primary producers of short-chain fatty acids (SCFAs) such as butyrate, which help maintain the integrity of the gut's epithelial lining by supporting tight junction protein expression.[1] Their depletion in the y-PAN cohort raises the question of compromised barrier integrity, a state in which bacterial byproducts are more able to translocate into systemic circulation and provoke an inflammatory cytokine response.[2] This inflammatory signal is not confined to the gut; there is growing evidence that it can extend to the central nervous system, provoking neuroinflammatory activity that offers a plausible physiological bridge between the microbial disruption these authors observed and the neuropsychiatric presentation itself.[3] This same breakdown in barrier integrity has also been associated with the development of food sensitivities. When the gut lining is compromised, larger dietary proteins are able to pass through that would normally be blocked or safely tolerated – and the immune system may begin treating them as foreign antigens rather than harmless dietary proteins. As a result, children may start reacting to foods that previously caused no issue, further compounding the inflammatory and symptom burden.[4] Addressing this thread clinically often falls to an integrative provider trained in structured gut-restoration protocols such as the 5R protocol (Remove, Replace, Reinoculate, Repair, Rebalance), which offers a systematic approach to reducing gut-derived inflammatory triggers alongside the multidisciplinary medical management these children require.[5]

Beyond the gut microbiome itself, hypothalamic-pituitary-adrenal (HPA) axis dysregulation deserves its own clinical attention as both a contributor to, and consequence of, this presentation. Cortisol fluctuation associated with HPA dysregulation has documented effects on mucosal integrity, including suppression of gut secretory IgA (sIgA) and impaired synthesis of structural proteins within enterocytes. These physiologic factors compound the barrier compromise discussed above.[6] The direction of cortisol dysregulation matters clinically: a hypercortisol state has a well-documented immunosuppressive, blunting effect, while the chronic or depleted phase that often follows prolonged stress or illness is associated with impaired cortisol output and a corresponding loss of the immunomodulatory brake on inflammatory and autoimmune processes.[7] Given that PANDAS itself is hypothesized to arise through a molecular mimicry mechanism, in which streptococcal antibodies cross-react against neuronal targets,[8] this loss of immune restraint during chronic HPA exhaustion may plausibly amplify the very autoimmune process underlying the disorder. In the pediatric population specifically, this axis is rarely given the chance to rest: children are navigating a near-constant stream of developmental and psychosocial change. These stimuli are often reported as new academic pressures, shifting friendships, sibling dynamics, family stress – any of which can activate the same HPA cascade described above, and each of which has been independently associated with symptom exacerbation in pediatric neuropsychiatric and tic populations.[9]

Cortisol dysregulation also reaches beyond immune and mucosal effects into the central nervous system, where it influences several neurotransmitter systems implicated in anxiety, including serotonin and GABA.[10] Dopamine, however, warrants particular attention here, as it is the very system the reviewed authors identified as compromised in the PANS/PANDAS gut ecology. This creates a dual, compounding pathway toward reduced dopaminergic tone: the gut-derived route already discussed, in which Firmicutes depletion limits the microbiome's capacity to support dopamine precursor synthesis, and a second, centrally-mediated route, in which chronic cortisol dysregulation directly impairs dopaminergic transmission.[11] Because dopamine plays a key role in how the brain processes and calibrates threat,[12] a nervous system compromised from both directions at once is left less equipped to regulate that response appropriately, and is clinically manifesting as heightened anxiety. This matters beyond the symptom itself: in pediatric tic populations, psychosocial stress and anxiety have been shown to independently predict worsening tic severity over time,[9] suggesting that anxiety in these children is not merely a symptom to note, but an active driver that can exacerbate the broader PANS/PANDAS presentation.

For the integrative provider, this points toward the value of cortisol testing to characterize the specific phase of HPA dysregulation present. From there, a multi-pronged approach to HPA-axis support is warranted. This may include targeted adaptogenic botanicals and regulating nutrients, neuro-emotional support such as counseling or therapy, and broader lifestyle intervention addressing the child's actual stress load and ambient living environment. Together, these strategies serve as a complement to the gut-focused interventions discussed above.

Beyond addressing the biochemical and physiological drivers underlying PANS/PANDAS, the chiropractor's role in recognizing and appropriately managing this presentation cannot be overstated. The Doctor of Chiropractic is accessible to children and adolescents and may serve as an initial point of contact for pediatric patients.[13,14] Many families seek chiropractic care first, and often present with musculoskeletal complaints that are in fact secondary to non-mechanical drivers such as neurological, infectious,

inflammatory, autoimmune, or systemic disease. As such, proficiency in differential diagnosis, red-flag identification, and appropriate referral is a core component of the chiropractor's scope of practice. This is reflected in practice: an international survey found that 81.2% of chiropractors reported referring pediatric patients to other providers when appropriate.[15]

A pediatric patient may present to a chiropractic office with musculoskeletal pain or motor complaints that appear mechanical in nature. These symptoms may have a mechanical onset or be complicated by other non-mechanical issues related to previous infections, such as the streptococcal infections seen with PANS/PANDAS. Common presentations include spine or extremity symptoms, diffuse myofascial pain or tenderness, headaches, and TMJ symptoms.[16] Some children may also demonstrate gross or fine motor weakness, slouched posture, or poor coordination. Sudden changes in handwriting or the development of dysgraphia can be a particularly useful historical clue to an acute change in fine-motor function. Motor tics may be perceived initially by a parent as a musculoskeletal or behavioral issue which may alter normal activities.[16,17,19]

These findings are nonspecific and should not independently be considered evidence of PANS/PANDAS. Their clinical significance increases when a musculoskeletal or movement complaint occurs in association with the abrupt onset of obsessive-compulsive behaviors or severely altered dietary intake, accompanied by other neuropsychiatric changes such as severe anxiety, mood changes, tics, sensory disturbances, sleep disruption, urinary changes, deterioration in school performance, or sudden changes in handwriting.[17,19] In a pediatric chiropractic setting, this combination should prompt expansion of the history, consideration of appropriate neurologic, inflammatory, rheumatologic, and infectious differential diagnoses, and referral for pediatric medical evaluation when indicated.[16,17]

A useful clinical approach, summarized in Table 1, includes a focused history covering neuropsychiatric and gastrointestinal red flags, a targeted neurologic exam, a clear co-management threshold, and guidance on continuing neuromusculoskeletal care where appropriate.[16]

Per American Academy of Pediatrics guidance, suspected PANS/PANDAS should prompt medical evaluation by a multidisciplinary team – pediatric medicine, neurology, psychiatry/psychology, infectious disease, and/or immunology.[17] It is worth noting that the chiropractor's assessment of these children should not be limited to a purely musculoskeletal lens. A growing body of neurophysiological research suggests that the chiropractic adjustment stimulates paraspinal afferent input capable of altering central nervous system processing and reflex output.[18] Within this framework, chiropractic care in this population is directed not at treating PANS/PANDAS itself, but at supporting more normal neurological expression – a neuromusculoskeletal (NMS), rather than strictly musculoskeletal (MS), perspective – making it a necessary consideration alongside the gut- and HPA-focused strategies discussed above and the multidisciplinary medical management these children require.

In closing, PANS/PANDAS represents a genuinely multi-systemic presentation, and the findings of Quagliariello et al. offer a compelling, if preliminary, biological thread

Domain	Assessment points
Neuropsychiatric history	Abrupt-onset behavioral change; new vocal/motor tics; new anxiety or emotional lability; sleep disturbance; academic decline; prior infection (esp. streptococcal)
Gastrointestinal history	Abdominal pain, diarrhea, constipation, reflux; recent dietary changes; antibiotic or probiotic use
Neurologic exam	Mental status/behavior observation; cranial nerves; motor exam; reflexes; coordination; gait; involuntary movements
Co-management threshold	Suspected PANS/PANDAS -> multidisciplinary referral (pediatric medicine, neurology, psychiatry/psychology, infectious disease, immunology)
Musculoskeletal management	Continue chiropractic care for coexisting neuromusculoskeletal (NMS) presentations; clearly distinguish the mechanical presentation from the PANS/PANDAS process itself

Table 1: Clinical assessment and co-management pathway for suspected PANS/PANDAS.

connecting gut microbial disruption to the neuropsychiatric symptoms these children display. For the practicing chiropractor, the clinical takeaway is threefold: first, recognize that the Firmicutes depletion and resulting barrier compromise identified in this population is not an isolated gut finding but a plausible contributor to the systemic and neuroinflammatory burden these children carry; second, appreciate that HPA axis dysregulation is not a downstream bystander but an active driver of both mucosal integrity and immune dysregulation, meriting its own clinical attention; and third, and perhaps most critically, understand that the chiropractor's greatest value in this population may not be the adjustment itself, but the clinical vigilance to recognize red flags early, coordinate with a multidisciplinary team, and support the child's care alongside, rather than in place of, appropriate medical management. A chiropractor equipped with this working knowledge is positioned not merely as a musculoskeletal provider, but as an informed member of the care team for one of pediatrics' most complex and evolving diagnoses.

Conflicts to Disclose

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