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CASE STUDY

GAPS Nutritional Protocol as a Treatment for PANDAS: A Case Study

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ABSTRACT

Background: PANDAS is a debilitating psychiatric condition that appears suddenly in childhood characterized by obsessive and compulsive behaviour, anxiety, fear, phobias, tics, irritability, mood swings, developmental regression, sleep issues and hallucinations. It is often hypothesized that this range of symptoms is caused by an autoimmune response to a Group A streptococcal infection. However, the exact aetiology remains elusive, and so do the mechanisms behind the heterogenous picture of this condition. Growing research is calling attention to the role of poor gut health in autoimmune conditions, psychological conditions, and neurological conditions – all of which are relevant to PANDAS. The gut microbiome is a perfect target for treatment as it is flexible and adapts quickly to changes. Currently, the first-line treatments for PANDAS are antibiotics and mood stabilizers. Yet, these are not viable as a long-term solution and often do not prevent further exacerbation of symptoms. The GAPS Nutritional Protocol aims to heal the gut lining, and restore microbial balance in the gut flora. Academic research using this protocol is scarce, despite numerous patients reporting healing from severe inflammatory, digestive, psychological, and neurodevelopmental conditions such as Autism, ADHD, mental illness, digestive illnesses and autoimmune disease.

Case presentation: The current case study aims to explore the GAPS Nutritional Protocol as a treatment for PANDAS in a 16-years-old patient. The patient was diagnosed with PANDAS at 12 years of age and was put on antibiotics and antipsychotics. Symptoms were present since early childhood and did not improve. He followed the GAPS Nutritional Protocol for 18 months after which all his symptoms disappeared. This qualitative observation was corroborated by objective data: eosinophils, neutrophils, lymphocytes, and mean platelet volume values all returned to normal ranges post-intervention, after years of aberrant results. PANDAS diagnosis was officially removed by his general practitioner and all medications were stopped.

Conclusions: Gut dysbiosis is an important element of PANDAS' aetiology and the GAPS Nutritional Protocol is a promising treatment of PANDAS. GAPS Nutritional Protocol is an effective strategy for PANDAS and other health problems linked to abnormalities in the gut microbiome.

BACKGROUND

First described in 1998, Paediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal infections (PANDAS) is a specific case of Paediatric Acute-onset Neuropsychiatric Syndrome (PANS) (Quagliarello et al., 2018). PANS is a 'later, broader iteration of PANDAS' (Wilbur et al., 2019, p. 85), that englobes various neuropsychiatric conditions that are triggered suddenly. The conditions are thought to be caused by infections, metabolic issues, and/or environmental factors (Swedo et al., 1998; Wilbur et al., 2019). Given the temporal association between the onset of symptoms and the group A streptococcal infection (GAS), it is often hypothesised that this range of symptoms is caused by an autoimmune response to the GAS infection (Sigra, Hesselmark, & Bejerot, 2018).

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PANDAS symptoms include obsessive and compulsive disorder (OCD), hypersensitivities, depression, insomnia, food restriction, hyperactivity, inattentiveness and in some cases, hallucinations. (Frankovich et al., 2015; Mangiola et al., 2016; Thienemann et al., 2017)

Due to the heterogeneity of its clinical picture, the PANDAS diagnosis is considered controversial, and the understanding of its aetiology remains elusive (Dale et al., 2006; Gamucci et al., 2019; Leckman et al., 2011; Orefici, Cardona, Cox, and Cunningham, 2016).

Similarly, treatment for PANDAS is a complex issue, as the symptoms encompass different areas of psychopathology. Various possible treatments that can be combined differently depending on the patient's profile: antibiotics, immunomodulatory therapy, tonsillectomy, cognitive and behavioral therapy, non-steroidal anti-inflammatory drugs, antidepressants, antipsychotics, and mood stabilizers (Thienemann et al., 2017). Despite some authors advocating the intake of antibiotics as first-line treatment (Calaprice, Tona, & Murphy, 2018), other studies remain skeptical as to their efficacy, tolerability, and long-term adequacy (Garvey et al., 1999; Sigra et al., 2018). Indeed, Murphy et al. (2017) suggested that antibiotics only alleviate OCD-related symptoms. Similarly, while antibiotics can be of assistance when a GAS infection is in action, there is no evidence supporting the effectiveness of antibiotic courses in preventing exacerbations of PANDAS symptoms (Wilbur et al., 2019). This supports findings of Quagliarello et al. (2018) who state that PANDAS' inflammatory condition 'is likely maintained in patients, even after the infection itself has resolved' (p.12).

In most cases, medications treat symptoms, not the underlying cause. Here, the question to ask is: where is the inflammation coming from and why does it persist? A comprehensive, case-by-case approach is vital, and should predominate when exploring PANDAS and its treatments (Sigra et al., 2018).

GUT HEALTH IN PATIENTS WITH PANDAS

Most research highlights the absence of biological markers for PANDAS (Gamucci et al., 2019). Yet, Quagliariello et al. (2018) have investigated the gut microbiota composition in a sample of 30 children suffering from PANDAS. The results suggest a relationship between PANDAS and gut flora composition. Younger participants displayed all the signs of gut dysbiosis. Their gut flora were less biodiverse than those of their control peers.

PANDAS participants displayed lower levels of clostridia and roseburia, bacteria that are critical in defending our bodies against external infections (Lopetuso, Scaldaferri, Petito, & Gasbarrini, 2013) and preserving both gut homeostasis and the gut barrier (Velasquez-Manoff, 2015). Finally, erysipelotrichaceae bacteria were missing from the microbiota of PANDAS participants. Interestingly, findings from Palm et al. (2014) and Kawikova et al. (2010) suggest a correlation between the absence of erysipelotrichaceae and immunologic disorders.

The above findings are crucial as they suggest not only that there might be biomarkers for PANDAS, but that these lie in the gut. This resonates with a growing concept in today's literature: the gut-brain axis.

Contrary to our genome, microbiota are flexible and responsive to environmental changes (Lloyd-Price et al., 2017). This makes our microbial inhabitants a potential target for treatment (Cryan et al., 2019). Concerning PANDAS, research has already demonstrated the validity of such an approach. For instance, in Calaprice, Tona, and Murphy's (2018) large sample, 352 families stated that alternative medicine treatments with probiotics, Omega 3, vitamin D, homeopathy and gluten-free diet improved their child's health state.

GAPS NUTRITIONAL PROTOCOL: THE DIET THAT FOCUSES ON YHE GUT-BRAIN AXIS

In the last two decades, Dr Campbell-McBride has developed a specific protocol that focusses on repairing the gut lining and restoring normal balance in the gut microbiome.

GAPS stands for Gut And Psychology/Physiology Syndrome. Its core principles rely on the need for a healthy microbiome for our body to function correctly.

The Full GAPS Diet eliminates all processed foods, sugar, vegetable oils, grains, starchy vegetables and legumes, and focusses on nutrient-dense foods such as healthy fats and stocks. The GAPS Introduction Diet is designed for deeper healing: it is a stage-by-stage introduction of nourishing foods, starting from the easiest-to-digest to more difficult-to-digest foods, slowly working up to The Full GAPS Diet. As it is crucial to replace the pathogens in our gut with beneficial microbes, probiotics are central to the protocol, both from fermented foods and commercial preparations (please see our companion article *GAPS Nutritional Protocol: how healing the gut removes the basis for all chronic diseases*, for a thorough description of the GAPS Nutritional Protocol).

Although the foundations of such a protocol have been accepted by the medical community for a long time (Campbell-McBride, 2020; Gottschall, 1994; Haas, 1951; Price, 2016), the scientific literature remains anecdotal. Throughout this case report, the current study aims to shed light on the validity of the GAPS Nutritional Protocol and highlight why this approach is fundamental for the treatment of PANDAS.

CASE PRESENTATION

Medical and Developmental History

George was born in 2000 through a C-section. He was breastfed for six months, after which he was weaned with homemade soups and, on rarer occasions, commercial homogenised foods.

As a child, George displayed signs of insecure attachment. He would follow both his parents all the time, and they struggled to leave him with other people or even on his own. His most common words were "mom don't leave me". Bedtime was complicated as George appeared to suffer from nightmares and night terrors. He also displayed disturbing digestive issues such as bloating, abdominal pain, and constipation. Mealtimes became problematic, as George was incredibly fussy with food.

At 12 years of age, his insecurities and anxieties became uncontrollable. He suddenly refused to go to school and was clearly overwhelmed by simple tasks. Tics emerged and he would make, as his mother described, "snake-resembling" movements.

For a year and a half, George had to drop out of school. He saw a therapist to whom he confessed all his emerging phobias and OCD-related symptoms. George was full of invasive negative thoughts that conditioned his daily life.

At 14 years of age, after years of questioning and researching, George's parents had concluded that their son might suffer from a disease called PANDAS. They went to another specialist, who confirmed this diagnosis. In addition, they also diagnosed George with an anxiety disorder. Antibiotic therapy was prescribed in combination with mood stabilizers.

The prescribed medication led to some improvements in eye contact and tics. However, this treatment did not have an impact on George's anxiety, aggressiveness, and reduced attention span.

When George was 15, his parents decided, in one last attempt, to try a nutritional intervention. They contacted Shantih Coro, a Registered Dietician, and Certified GAPS Practitioner.

Intervention

BEFORE INTERVENTION

George's diet prior to visiting Mr Coro consisted of a traditional Italian menu. George was a fussy eater; the only things that he ate gladly were sweets and processed carbohydrates. He refused vegetables, fruit, and animal products.

DURING INTERVENTION

Mr Coro recommended that George start immediately from the GAPS Introduction Diet. It was challenging for an Italian family to live without pasta, bread, pizza, and sugar, so during the first weeks George only removed some of these foods. Yet, his sleep and bowel movements significantly improved. This notable progress encouraged the family to persist with the protocol. For 30 days, George thoroughly followed the GAPS Introduction Diet, after which, all of his symptoms had improved, including the tics. This impressed the whole family deeply and inspired them to persevere with this approach. For six months, George went through the stages of The GAPS Introduction Diet, before transitioning to The Full GAPS Diet. After 18 months of following The GAPS Nutritional Protocol, the PANDAS diagnosis was removed, and all medication was stopped.

POST-INTERVENTION

Qualitative Observations: By following the GAPS Nutritional Protocol, George gradually saw all his symptoms disappear, to the point where the diagnosis was removed, and all medications were stopped. He went back to having a normal social and academic life, after years of communication and learning difficulties linked to his severe anxiety. He demanded, of his own initiative, to go back to public school (public school is harder in Italy, and the fact that George decided to go back by himself was another proof of his recovery). Nowadays, George does not follow the GAPS Diet, but he maintains healthy eating habits and lifestyle. He studies medicine with excellent grades.

Quantitative Analysis: George's healing following the GAPS Diet is also visible in objective, quantitative data (see Table 1).

Table 1. Critical blood test values throughout the GAPS Diet implementation

	Date			
	Apr 2016	Aug 2016	Jan 2018	Jan 2019
MPV	10.8 fL	10.7 fL	10.5 fL	10.2 fL
NEUT	40.40%	36.90%	48.%	54.60%
LYMPH	51%	55.80%	41.80%	34.90%
NLR	0.79	0.66	1.15	1.56
EO	3.30%	2%	3.10%	2.20%

Colour chart: Red cells indicate a significantly high value compared to the norm for the relevant age range; Blue cells indicate a significantly low value compared to the norm for the relevant age range; Green cells indicate a value within normal range.

Mean Platelet Volume (MPV): High MPV has been reported multiple times in cases of sepsis (Ates et al., 2015; Aydemir, Piskin, Akduman, Kokturk, & Aktas, 2015; Shaaban & Safwat, 2020) and has been explored as a biomarker for inflammatory and autoimmune diseases (Schmoeller et al., 2017; Soydinc et al., 2014; Yavuz & Ece, 2014; Yuri Gasparyan, Ayvazyan, Mikhailidis, & Kitas, 2011). In 2016, George's MPV was significantly high, which indicated that this patient had systemic infection, inflammation, and autoimmunity. Yet, the diagnosis of PANDAS was established in 2012, followed by intensive antibiotic treatments aimed at clearing any possible GAS infection. The child continued being ill until 2018, when, after the GAPS intervention, his MPV went back to normal, and the clinical picture showed disappearance of all symptoms of PANDAS.

N*eutrophils (NEUT) and Lymphocytes (LYMPH):* NEUT and LYMPH are central in the prevention of autoimmune diseases (Seeley et al., 2008). George's blood results revealed a significantly low percentage of NEUT in his bloodstream for over two years: this is called chronic neutropenia, which can be indicative of a suppressed autoimmune system and/or an autoimmune disorder (Akhtari, Curtis, & Waller, 2009; Boxer, Greenberg, Boxer, & Stossel, 1975; Boxer, 2012; Bruin et al., 1999; Kolaczkowska & Kubes, 2013; Starkebaum, 2002). After the GAPS intervention, George's NEUT count had returned to normal (see Table 1). George also displayed significantly high levels of lymphocytes, called lymphocytosis. Lymphocytosis is thought to be caused by bacterial, viral, or parasitic infections, cancers, and autoimmune disorders that lead to chronic inflammation (Hamad & Mangla, 2019). George's LYMPH percentage was out of the normal range and reflected an inflammatory state. After the GAPS Nutritional Protocol, his LYMPH count was restored to normal (see Table 1).

Neutrophil-to-Lymphocyte Ratio (NLR): George's blood results depicted a peculiar profile, one of a particularly low neutrophil-to-lymphocyte ratio (NLR) (Forget et al., 2017). Low NLR is associated with chronic inflammation, infection, and autoimmune conditions (Castoldi, Liso, & Aversa, 2014; Dursun, Ozsoylu, & Akyildiz, 2018) and has also been explored as a biomarker for OCD (a prevalent symptom in PANDAS). Uzun et al. (2020) have found an abnormally low NLR ranging between 0.89 and 1.87 in children and adolescents with OCD. In 2016, George's NLR at 0.66 was lower than the abovementioned range. Doctors had warned George's family that it might be impossible to revert this. Yet, post-intervention, George's NLR went completely back to normal (see Table 1).

Eosinophils (EO): A high EO count (eosinophilia) reflects autoimmune issues (Diny, Rose, & Čiháková, 2017; Kovalszki & Weller, 2016; Nagata, Nakagome & Soma, 2020; Wang, Lu, Guo, & Qian, 2009), severe inflammation and/or parasitic infections. Just like his other blood levels, his EO count decreased to a normal range after the GAPS intervention (see Table 1).

DISCUSSION

Key Findings

This case study aimed to explore the GAPS Nutritional Protocol as a treatment for PANS/PANDAS. Both qualitative and quantitative data indicated that George's condition improved following the GAPS Diet, conceived to heal and seal the 'leaky' gut lining and repopulate the gut flora with beneficial microbes.

After 18 months, George saw all his PANDAS-related symptoms disappear – tics, anxiety, hypersensitivity to noise and odours, sleep issues, concentration issues, fine motor issues, digestive issues, restricted eating habits, and quality of eye-contact – to the point where his diagnosis was officially removed.

In addition, the abnormal blood test results that were indicative of the PANDAS condition – EO, NEUT, LYMPH, NLR, MPV – were restored to normal ranges after the GAPS intervention.

Interpretations

Quagliarello et al. (2018) have claimed that PANDAS patients suffer from gut dysbiosis. The current study corroborates these findings and suggests that gut health is central to the treatment of PANDAS.

How did the GAPS Nutritional protocol help George heal from PANDAS?

When George followed the GAPS Nutritional Protocol, his family focussed on removing toxicity from his environment and his food. Removing all sugar, beans, grains, starch, and processed foods re-balanced George's gut microbiome. Homemade fermented dairy and fermented vegetables helped strengthen his beneficial flora. Food began to be correctly digested and absorbed. In addition, removal of fibre for a period of time (nuts, beans, fruit and raw vegetables) allowed his gut lining to heal. Nourishment from meat stocks and nutrient-dense animal foods – most importantly, collagen – sealed his 'leaky' gut. Healthy animal fats and cholesterol-rich foods provided him with the necessary building materials to reinforce every cell in his body and nourish his brain.

Where did George's gut dysbiosis come from?

Gut dysbiosis is inherited from our parents. George's mother has likely passed on a toxic load and compromised gut flora to her baby, as she herself suffered from candidiasis at a young age. She also suffered from anxiety during her adolescence. Furthermore, George was born through C-section and was only breastfed for six months. This did not give George's body the necessary tools to develop a strong immune system (Ip et al., 2007; Le Huërou-Luron, Blat, & Boudry, 2010; Neu & Rushing, 2011; Tannock et al., 2013).

The relationship between gut dysbiosis and PANDAS

PANDAS has been defined as an autoimmune disease (Swedo et al., 1998), and the gut microbiome is increasingly being considered crucial in development of autoimmunity (Belkaid & Hand, 2014; Cénit et al., 2014).

As suggested by Dr Campbell-McBride through her GAPS Nutritional Protocol, the source of autoimmune issues is gut dysbiosis, which damages the gut wall, causes abnormal digestion and absorption of food, and generates a flow of toxicity, while the body is unable to handle toxins from the environment (please see our companion article *GAPS Nutritional Protocol: how healing the gut removes the basis for all chronic diseases*, for further details). The immune system responds to all of these threats. Abnormal blood changes, which George displayed, were a consequence of his body reacting to undigested foods and toxins absorbing through the damaged gut wall (Nanagas & Kovalszki, 2019; Talley, 2008).

The effects of this toxicity on the brain lead to an 'abnormality in processing sensory input' (Campbell-McBride, 2010, p.338), commonly referred to as sensory processing disorder (SPD) in the autistic population (Clayton et al., 2018)

All GAPS people – people whose health issues stem from their damaged gut – experience SPD. In fact, many of George's symptoms were the immediate result of an SPD: his phobias, his hypersensitivity to noise and odours, his restricted eating behaviours, and his attention deficit. With the GAPS Nutritional Protocol these symptoms of SPD disappeared.

Sleep disturbances are a dominant symptom of PANDAS and George was particularly prone to these. In their recent study, Smith et al. (2019) suggested that a more diverse microbiome is associated with better quality of sleep. Since young people diagnosed with PANDAS appear to have less biodiverse gut flora than their peers (Quagliarello et al., 2018), gut health could explain this aspect of PANDAS. In addition, Quagliarello et al. (2018) found that tyrosine levels were particularly low in their PANDAS sample. Tyrosine is a precursor of dopamine, which plays an important role in circadian rhythms (Korshunov, Blakemore, & Trombley, 2017).

George's anxiety and psychotic symptoms significantly dropped once his microbiome found a better balance and once his body was nourished with nutrient-dense food. This resonates with past research suggesting gut health and mental sanity are intrinsically linked (Cade et al., 1990; Calabrese, Rapport, & Shelton, 1999; Dohan, 1966; Dohan & Grasberger, 1973; Hoffer, 1971; Kaplan, Crawford, Field, & Simpson, 2007; Singh, 1976; Torrey et al., 1984)

CONTRIBUTIONS

Although widely used by patients around the world with promising results, the GAPS Nutritional Protocol has been scarcely studied in academic scientific literature. Among the few studies which have looked at the GAPS Nutritional Protocol (Abele, Tzivian, Meija, & Folkmanis, 2019; Babinska et al., 2020; Cekici & Sanlier, 2019; Çikili, Deniz, & Çakal, 2019; Nazarenkov et al., 2018), no research has explored it as a treatment for autoimmune diseases such as PANDAS.

We believe our case study fills recent research's stated gaps when it comes to understanding PANDAS (Dale et al., 2006; Gamucci et al., 2019; Leckman et al., 2011; Orefici et al., 2016; Sigra et al., 2018).

FURTHER RESEARCH

Given the lack of studies evaluating the effectiveness of the GAPS Nutritional Protocol treatment, we highly encourage researchers interested in addressing gut dysbiosis as the cause of psychological and/or physiological disorders to use the GAPS Nutritional Protocol in their practice and/or empirical studies.

CONCLUSION

The current study aimed to explore the GAPS Nutritional Protocol as a treatment for PANDAS. After nine months on the GAPS Diet, George's symptoms had significantly improved. After 18 months, they had disappeared, to the point where his diagnosis was officially removed by medical authorities and all medications were stopped. The healing was also visible in important blood analyses such as mean platelet volume, neutrophil count, lymphocyte count, and eosinophil count, which despite being significantly out of range for multiple years, all returned to normal values after George followed the GAPS Nutritional Protocol. This case study suggests gut dysbiosis could be at the centre of PANDAS' aetiology and that gut health should be given more consideration when it comes to treating autoimmune diseases.

DECLARATIONS

Ethics Approval and Consent to Participate

Not applicable. The study is retrospective. The patient engaged in the GAPS Nutritional Protocol willingly, i.e., they were not prompted by researchers for the purpose of the article. For privacy reasons, George is a pseudonym.

Consent for Publication

Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient. A copy of the consent form is available for review by the Editor of this journal.

Availability of Data and Materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. Dr Natasha Campbell-McBride is the creator of the GAPS concept and the GAPS Nutritional Protocol.

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Authors' Contributions

Shantih Coro collected the data. Sophie Delaunay-Vagliasindi collected additional qualitative data, analysed all data, and wrote the manuscript. Natasha Campbell-McBride and Stephanie Seneff supervised and edited. All authors read and approved the final manuscript.

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This case was written following the CARE guidelines.

Author's Information

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