Clinical Experience of Integrative Autism Treatment with Manual Lymphatic Drainage

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Abstract

In this study we report the results of a protocol for improving brain lymphatic flow in autism through lymphatic drainage massage, a technique successfully used in a variety of conditions where intracranial lymphatic circulation is hampered by obstacles at the level of deep cervical nodes. At the end of May 2018, the Biomedical Centre for Autism Research and Treatment started implementing a protocol of manual lymphatic drainage of the deep cervical nodes on autistic subjects. By October 2018, several scores of patients had been treated with this protocol. In this report, we describe the cases of three autistic patients for whom manual lymphatic massage was remarkably effective. To our knowledge, this is the first report of lymphatic drainage massage at the level of the deep cervical nodes in autism. Symptomatic improvement was robust and we attribute these results to the effects of the massage on the intracranial lymph or sometimes referred to as the glymphatic circulation with improvement of brain lymphatic drainage believed leading to a decrease of neuroinflammation. In addition to stimulating lymphatic drainage, we postulate that the protocol may serve also as vagus nerve stimulation. The protocol also targets the larynx in a manner similar as described for laryngeal manual therapy for the treatment of dysphonia, and this factor may be contributing to the overall improvement of symptoms, with particular reference to speech. Based on the cases described in this report and on our ongoing research, we are convinced that this type of inexpensive, harmless and easy-to-implement approach of manual lymphatic drainage can be beneficial to autistic patients and represents a new and promising treatment. We expect that the described protocol will play a central role in future treatments for autism, both alone and in combination with other therapies such as behavioral therapies or nutritional interventions.

Keywords: Autism; Brain Lymphatic System; Massage; Vagus Nerve; Larynx

Introduction

Autism is a complex neurodevelopmental disorder where genetic, environmental, immunologic, and metabolic noxae may contribute to the onset and progression of the disorder. Each of these factors probably plays a different role in each individual, contributing to the heterogeneity of symptoms [1]. Similar to other complex chronic conditions of multifactorial origin, it is doubtful that one single cause for autism can be identified and, therefore, the search for one single treatment targeting the hypothetical "cause" of autism may prove fruitless. The search for different etiologic agents may prove useful in preventing the disorder; however, treatment may prove more successful if it is intended to target the pathogenesis of autism rather than its etiology. In this context, autism may share similarities with cancer, both being chronic, self-sustaining conditions regardless of etiology.

Elimination of known causes, for example, cigarette smoking, helps reduce lung cancer incidence. However, when lung cancer occurs, in smokers or non-smokers, therapy needs to address the pathogenesis of the disease. That means trying to stop proliferation of cancer cells, rather than focusing on the cause of the disease (for rev. on the similarities between autism and cancer, see Ruggiero and Pacini [2]).

In an attempt to contribute to the understanding the pathogenesis of autism and to targeted treatments, we demonstrated in 2014 that brains of autistic children show peculiar lesions, defined as cortical dysplasia, with extra-axial fluid accumulation, findings which significantly correlated with the severity of symptoms [3]. In 2015, we published a paper hypothesizing that cortical dysplasia and extra-axial fluid accumulation in autism were associated with, and possibly caused by, impaired brain lymphatic drainage through the deep cervical nodes [4]. According to this hypothesis, common infections or inflammatory processes involving the mouth, ears, nose and throat involve the deep cervical nodes, a common occurrence that is evidenced by enlarged palpable nodes that can be studied by ultrasonography (Figure 1).

**Figure 1:** Ultrasonographic appearance of a deep cervical node and its relation with the vagus nerve. The image shows an enlarged, inflamed, deep cervical node that sits in the angle formed by the common carotid artery and the internal jugular vein, anteriorly to the vascular structures. The hyperechoic hilum of the node is clearly visible. The oval, elongated, shape and the presence of the hyperechoic hilum are characteristics of inflamed and not neoplastic nodes. The longest diameter of the node, measured at the time of the ultrasonography using calipers (D1), is 0.80 cm. The vagus nerve appears as a small triangular structure located posteriorly inside the carotid sheath between the common carotid artery and the internal jugular vein; it shows an internal honeycomb structure. The reference bars on the right of the image indicate depth from the skin surface; the node and the vagus nerve are separated by few millimeters. This image is from the personal archive of one of the Authors and is presented to show the relation between deep cervical nodes and the vagus nerve; it does not refer to any of the three clinical cases presented in this study.
Engorgement of the deep cervical nodes, as a consequence of infectious or inflammatory processes of the mouth, ears, nose and throat, represents an obstacle to lymph flow including the lymph coming from the brain through the meningeal lymphatic system [5]. Impaired drainage of lymph from the brain would then be responsible for the cortical dysplasia and extra-axial fluid accumulation that we had observed in the brains of autistic children, and may therefore contribute to the pathogenesis of the autism spectrum disorder since impaired drainage of brain lymph is responsible for neuroinflammation [6], a ubiquitous finding in autism [7].

Indirect evidence of a connection between otorhinolaryngologic infections and autism can be found in the clinical observation published by Matarazzo in 2002. In this paper, the Author describes two cases of children who at first developed normally, but, before the age of three, developed autistic symptoms following the reactivation of a chronic otorhinolaryngologic infection. In one case, anti-inflammatory/immunosuppressive treatment performed in the first months of the disease led to a complete cure, whereas in the other case, treated only six years later, treatment showed a partial but definitive improvement [8]. It is worth noting that in 2002 the existence of the brain lymphatic system was unknown. However, today we may postulate that the anti-inflammatory/immunosuppressive treatment performed by Matarazzo led to resolution of the engorgement of the deep cervical nodes associated with otorhinolaryngologic infection, thus reestablishing the flow of lymph from the brain. The observation by Matarazzo, reinterpreted by our hypothesis, is consistent with another concept that predates the description of the brain lymphatic system, that is, the clinical significance of cerebrospinal fluid stasis in the development of autism spectrum disorder [9].

Based on the observation and our hypotheses described above, we designed a simple protocol aimed at improving brain lymphatic flow in autism through manual lymphatic drainage massage, a technique successfully used in a variety of conditions where lymphatic circulation is hampered by obstacles at the level of deep cervical nodes. Manual lymphatic drainage is a known effective treatment for decongesting lymph nodes and is recommended, for example, in the treatment of lymphedema following breast cancer therapies [10]. An extensive review of the efficacy and safety of manual lymphatic drainage in breast cancer patients recently concluded that such a technique is safe and offers additional benefits to other techniques aimed at reducing swelling [10]. Interestingly, there are other observations indicating that massage may prove helpful in autism [11] although, in those studies, the massage was not performed with the goal of decongesting the deep cervical nodes.

At the end of May 2018, the Biomedical Centre for Autism Research and Treatment started implementing a protocol of manual lymphatic drainage of the deep cervical nodes on autistic subjects with the goal of assessing its efficacy on clinical outcomes. By October 2018, several scores of patients have been treated with this protocol; here, we describe the cases of three autistic patients for whom the treatment was remarkably effective.

Patients and Methods

At the Biomedical Centre for Autism Research and Treatment, strategies targeting the immune system and neuro-inflammation are routinely implemented with the goal of improving symptoms and quality of life of autistic subjects. In addition to pharmacological therapies or nutritional strategies [12] tailored to the needs of each individual, a protocol of manual lymphatic drainage of the deep cervical nodes has recently been introduced where parents are taught how to perform the massage on the autistic subject.

Methods

The protocol is based on manual massage that is performed using a commercial, petroleum-free, cosmetic cream with specific rheological and sensory properties containing vegetable oil, water, phosphatidylcholine from sunflower, chondroitin sulfate and a probiotic blend of *Bifidobacteria* and kefir grains (Sophia Flow, Woodinville, WA, USA). Use of a cream with specific rheological and sensory properties was chosen based on the evidence that massage is more effective with the use of ointments. For example, massage therapy is known to facilitate sleep in adults and infants, and it has been demonstrated that, in this context, it is more effective with oil versus no oil [13]. Likewise, with sunflower oil versus no oil, moderate pressure massage led to greater increases in weight in preterm neonates who were low birth weight, thus supporting the notion that ointments enhance the efficacy of massage [14]. The protocol consists in retrieving a small amount of the cream, about a chickpea size, with a disposable spoon (or other clean, disposable means) and rubbing it between...
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both hands until the cream warms up to increase its fluidity. The subject is then asked to overextend the neck tilting the head as far back as possible and the parent performs the massage with both hands, massaging the areas of the neck on the sides of the trachea with open palms and extended fingers. The parent is instructed to start from the top, with the tip of the fingers touching the jaw bone and, with light pressure, like brushing, slide the fingers down until they touch the base of the neck. The direction of massage is exclusively cranio-caudal, taking care to almost join the hand as they go down so to perform a sort of laryngeal manual massage. Parents are instructed to perform the massage before bedtime every day.

Patients

Diagnostic criteria for autism adopted at the Biomedical Centre for Autism Research and Treatment are:

1. Marked impairment in the use of multiple nonverbal behaviors such as eye-to-eye gaze, facial expression, body postures, and gestures to regulate social interaction.
2. Failure to develop peer relationships appropriate to developmental level.
3. Lack of spontaneous seeking to share enjoyment, interests or achievements with other people (e.g., by a lack of showing, bringing or pointing out objects of interest.
4. Lack of social or emotional reciprocity.
5. Delay in, or total lack of, the development of spoken language.
6. In individuals with adequate speech, marked impairment in the ability to initiate or sustain a conversation with others.
7. Stereotyped and repetitive use of language or idiosyncratic language.
8. Lack of varied, spontaneous, make-believe play or social imitative play appropriate to developmental level.
9. Encompassing preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal either in intensity or focus.
10. Apparently inflexible adherence to specific nonfunctional routines or rituals.
11. Stereotyped and repetitive motor mannerisms (e.g. hand or finger flapping or twisting, or complex whole-body movements).
12. Persistent preoccupation with parts of objects.

All patients described in this study met six or more criteria from this list, and had been diagnosed by either a child neurologist or developmental psychologist, in addition to receiving the evaluation of the clinician at the Biomedical Centre for Autism Research and Treatment.

No significant changes were made to the participants’ treatments apart from the introduction of the manual lymphatic drainage protocol during the timeframe reported in this study. The original clinical records as well as the informed consents given by patients or their parents or legal guardians, are conserved at the Biomedical Centre for Autism Research and Treatment. Since this is a low-number case report (that is, the case describes three or fewer cases) that does not produce generalizable knowledge, nor an investigation of an FDA regulated product, Institutional Review Board (IRB) review is not required for this activity [15].

The period of observation to which this study refers spanned six months of daily manual laryngeal massage (May-October, 2018). Two patients were male; Patient 1 was 2 years and 9 months, and Patient 3 was 6 years and 6 months old. One patient (n.2) was female, 9 years old. Concurrent pathologies of each patient are described in the following section.

Case Report

Patient 1: Male, 2 years and 9 months old at the time of implementing the manual lymphatic drainage protocol. The patients showed first signs of autism at 20 months of age when he lost the few words he had learned, lost eye contact, stopped responding when called,

and began bizarre behaviors - motor stereotypies - that included flapping. Subsequently, this patient developed crises of anger and violent tantrums, in particular when contradicted. The patient did not show significant bio-humoral alterations with the exception of slightly elevated platelet count and IgE. The patient had frequent bowel movements with very soft and hypocholic feces. Three days after implementation of the manual lymphatic drainage protocol, the patient spontaneously begun speaking a few words and eating without the need of assistance, properly using the tableware. Bowel movement were reduced to two movements per day with well-formed feces. The patient begun showing curiosity toward new foods and flapping progressively disappeared. In the following two months, he significantly increased the complexity of his vocabulary and the ability to appropriately follow complex instructions. Stereotypies disappeared and ability of learning during behavioral therapies significantly improved.

**Patient 2:** Female, 9 years old at the time of implementing the manual lymphatic drainage protocol, with confirmed diagnosis of early-onset autism and recurrent allergic asthma requiring desloratadine treatment. The most prominent autism symptoms were motor stereotypies, speech limited to very simple sentences, and significant delay in learning. Immediately after implementation of the manual lymphatic drainage, a slight, temporary, enlargement of latero-cervical nodes lasting for a few days was noted, possibly due to mobilization of lymph. Evident improvement of autistic symptoms consisted in spontaneous, faster and easier learning at school with increased alertness and focus. Ability in performing coordinated fine movements significantly increased and the patient began to write; this in turn resulted in increased self-esteem. Motor stereotypies significantly decreased and personal autonomy significantly increased.

**Patient 3:** Male, 6 years and 6 months old at the time of implementing the manual lymphatic drainage protocol. The patients showed first signs of autism at 15 months of age when he stopped developing speech, lost eye contact, stopped responding when called and refrained from social interactions. A diagnosis of atypical autism with hyperactivity and attention deficit was proposed at the age of 5. The child had chronic allergic rhinitis and sinusitis with persistent nasal congestion that caused open mouth breathing. The patient was very selective in his eating habits and only ate a few types of fried foods. Following implementation of the manual lymphatic drainage protocol, chronic nasal congestion was rapidly resolved, and nose breathing was reestablished. Eating habits were significantly improved and the patient began eating a variety of healthier foods. The patient also showed improvement in socialization; began to look at other children, trying to imitate their actions. Also, significant improvements in speech were observed with the patient speaking more complex sentences with better pronunciation.

**Discussion**

To our knowledge, this is the first report of implementation of a manual lymphatic drainage protocol at the level of the deep cervical nodes in autism. Since this clinical case report is an open-label, non-controlled, retrospective analysis, caution must be exercised when ascribing cause and effect to any treatment outcome. In addition, many of the behavioral outcome observation was parent-reported, which can be biased by parental expectations. However, despite these limitations, it appears that the response to manual lymphatic drainage protocol was robust with regard to symptomatic improvements and we attribute these remarkable results to the effects of the massage on the circulation of lymph with consequent improvement of brain lymphatic drainage possibly leading to decrease of neuroinflammation. Future studies will evaluate changes of markers of neuroinflammation and how they relate to symptom improvement following manual lymphatic drainage of the deep cervical nodes.

In addition to stimulating lymphatic drainage, we postulate that the protocol described here may serve also as vagus nerve stimulation. The deep cervical nodes are anatomically located in proximity of the vagus nerve in the neck and manual stimulation may target both the lymphatics and the vagus nerve. Figure 1, shows an example of ultrasonography of the neck where the proximity of an enlarged node to the vagus nerve is evident, and where the short distance between the skin and the lymphatic and nervous structures of the neck is also evident. The working hypothesis concerning the effects of manual lymphatic drainage on vagal stimulation is based on the

observed improvement of symptoms. Thus, it is well accepted that autism is marked by low vagal activity that results, among other symptoms, in gaze aversion and flat facial expressions. Consequently, vagal stimulation through massage may prove effective in improving the symptoms of autism [16] and may explain some of the clinical outcomes we reported in this study. In the case of the protocol described here, vagal stimulation may be achieved along with lymphatic drainage, thus targeting two prominent pathogenetic mechanisms at work in autism. In addition, this type of massage targets the larynx in a manner similar to that described for laryngeal manual therapy for the treatment of dysphonia [17]. It is worth noting that, despite the abundance of studies on autism, we found only 8 published papers in PubMed upon searching for the words “autism and larynx”, and none using “autism and laryngeal manual therapy” (search performed in November 2018). Such an observation was somehow surprising as alterations of speech are ubiquitous in autism. Indirect evidence on the role of the larynx in autism may be deduced from a single case report describing a 14-year-old autistic boy, with untreatable vocal tics, operated with lateralization (type IIB) thyroplasty. Interestingly, in addition to the expected reduction in tic frequency and intensity, the boy improved his ability to converse with his peers, participate in school activities, and even improved nutritional status, therefore showing an overall improvement of symptoms that went well beyond the limits of the organ [18].

In our experience, use of a cream with specific rheological properties proved instrumental in achieving the results reported above. This observation of ours is confirmed by others who have demonstrated that oily ointments increase the effectiveness of massage, in particular in infants, and produce effects that can be appreciated in a few days. For example, Taheri., et al. recently demonstrated that a short course of moderate pressure sunflower oil massage for only five days increases preterm infants’ weight gain and decreases their duration of neonatal intensive care unit stay significantly, possibly because of vagal stimulation [19].

In describing these individual cases, we are well aware that these reports, because of their heterogeneity, can be considered anecdotes. However, it is worth noting that a recent study on the evaluation of clinical practice prompts for re-evaluation of individual cases such as those presented here [20]. Thus, it is well known that some studies present large and impressive statistics obtained from many observations while others report a small number of noteworthy events, as we do in this study. According to the novel, authoritative, epistemological approach, “all of these stories become evidence of what works in medicine” [20] as appears to be the case for the report by Matarazzo on the association between otorhinolaryngologic infections and autism [8], or the case on improvement of autism symptoms following surgery of the larynx [18]. Therefore, we suggest that the clinical cases reported here may be considered as evidence for the effectiveness of manual lymphatic drainage protocol at the level of the deep cervical nodes in autism and may encourage further studies on this topic.

Conclusions

Based on the cases described above and on our ongoing experience, we are convinced that this type of inexpensive, harmless and easy-to-practice approach of manual lymphatic drainage can be of benefit to autistic patients and represents a new and promising treatment. We expect that the described protocol will play a central role in future treatments of autism, both alone and in combination with other therapies, such as behavioral therapies or nutritional interventions.

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Conflict of Interest
Nicola Antonucci is the founder of the Biomedical Centre for Autism Research and Treatment, a private clinic. Marco Ruggiero is the inventor of a number of supplements and, together with Stefania Pacini, developed the cream used for the manual lymphatic drainage described in this study. Neither he, nor Dr. Pacini, had any prior knowledge of the therapies being used nor of the names of any patient whose clinical outcomes were being analyzed and described in this study.

Authors’ Contributions
Nicola Antonucci: Performed all diagnostic and therapeutic procedures, evaluated patients and reported the clinical results here described.

Marco Ruggiero and Stefania Pacini: Wrote the first draft of this paper, provided critical input and assisted in revising and improving the paper. All authors have read and approved the manuscript.

Ethics
This article is original and contains material that has not been published in any scientific journal.

Advisory
No information in this paper is presented by the authors as medical advice. Caregivers, researchers and interested parties should research all information given. Beginning any significant biomedical or other interventions that may impact physiology, or making any changes to an established regimen should be discussed with the patient’s physician in advance. Standard of care for each pathology must be followed as well as rules and regulations established by Health Authorities of each Country.

Bibliography

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