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Innovative interventions: neuromodulation to enhance motor learning in autism

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NEUROMODULATION TO ENHANCE MOTOR LEARNING IN AUTISM

by

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DEDICATION

To the love of my life, who has inspired me to reach for my fullest potential.

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INNOVATIVE INTERVENTIONS:

NEUROMODULATION TO ENHANCE MOTOR LEARNING IN AUTISM

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ABSTRACT

Autism spectrum disorders are best understood as a complex set of symptoms that impact social, communication, and behavioral skills. Autistic brains have abnormalities in the anatomy, neural architecture, cytoarchitecture, and neurotransmitter systems (Bharath et al., 2019; Dicarlo & Wallace, 2022; Fatemi et al., 2012; Friedman et al., 2006; Karvat & Kimchi, 2014; Xu et al., 2020). This unique neurology may partially explain why motor impairments are so widespread in this population. Motor impairments are present in up to 88% of autistic people, emerging in early life and persisting into adulthood (Kangarani-Farahani et al., 2023; Liu et al., 2014). These deficits exert a cascading impact, contributing to impairments in daily living skills (Miller et al., 2024; Ozboke et al., 2021; Travers et al., 2022). Creating motor phenotypes that describe how a person's physiology relates to their unique neurology may help with developing more effective interventions. This program investigates the correlation between biomarkers and psychomotor measures in autistic children. From there, an adjunct intervention is deployed to improve neuromodulation while engaging in motor learning. The goal is to move the field of occupational therapy towards a more precise and effective delivery model in order to achieve greater gains with less dosing of therapy.

PREFACE

Occupational therapy has the unique role of celebrating our clients for their individuality while problem-solving with them to create the life they want. As an occupational therapist who is board-certified in pediatrics and has worked for over two decades in the field of autism, the author is honored to serve children and their families in this role. The author's mission is to innovate, implement, and promote interventions that improve the lives of the children occupational therapists serve. In pursuit of this mission, the author has formulated a program derived from several different disciplines and practices that are not traditionally seen as being within the scope of occupational therapy. Innovative interventions often face resistance, but the author is inspired by the famous quote by Theodore Roosevelt:

> It is not the critic who counts; not the man who points out how the strong man stumbles, or when the doer of deeds could have done them better. The credit belongs to the man who is actually in the arena, whose face is marred by dust and sweat and blood; who strives valiantly; who errs, who comes short again and again, because there is no effort without error and shortcoming; but who does actually strive to do the deeds; who knows great enthusiasms, the great devotions; who spends himself in a worthy cause; who at the best knows in the end the triumph of high achievement, and at the worst, if he fails, at least fails while daring greatly… (Roosevelt, 1910, as cited in The Theodore Roosevelt Center at Dickinson State University).

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CHAPTER ONE – Introduction

Autism is a neurodevelopmental disorder diagnosed by differences in social and communication skills, as well as differences in behaviors/ interests (American Psychiatric Association, 2013). Missing in the diagnostic criteria are the motor differences observed in the majority of people with autism. Research has demonstrated that up to 88% of autistic people have motor impairments (Bhat, 2020; Kangarani-Farahani, et al., 2023; Licari et al., 2020). These differences are observable at a very young age and persist into adulthood (Miller et al., 2024). Also, these impairments negatively impact the ability to successfully participate in daily living skills (Ozboke et al., 2021; Travers et al., 2022). As such, occupational therapy practitioners (OTPs) are commonly a part of the treatment team for children with autism (Benevides et al., 2022).

Given the prevalence of motor impairments in this population, the evidence base in occupational therapy should be robust to guide interventions. However, a search of the literature reveals that in the last ten years, only 13 experimental, occupational therapy articles targeting motor skill interventions in autistic subjects have been published (Ajzenman et al., 2013; Alaniz et al., 2017; Alkhalifah et al., 2022; Collins et al., 2015; Hilton et al., 2014; Hirschmann et al., 2023; Iwanga et al., 2014; Jin et al., 2023; Kumar & Nagalakshmi, 2023; Lopez & Kume, 2018; Nuntanee & Daranee, 2019; Schoen et al., 2020; Walsh et al., 2021). Not only is the volume of the evidence base shallow, but the quality of the evidence is poor. Three of the 13 studies are poster presentations and one is a research platform from conference proceedings. The remaining nine published studies rarely describe the theory base informing the interventions, identify the key ingredients, or state the proposed mechanism of action. This limits the ability of OTPs to extrapolate information from the evidence to their clinical population. In addition, the wider field of research, including other disciplines such as physical therapy, applied behavior therapy, and physical education, have similar limitations despite a larger volume of studies.

Autistic Neurology and the Contribution to Motor Development

To further complicate matters, autism is a complex condition with a unique neurological profile. Autistic brains have abnormalities in the cortex both with the anatomy and the neurotransmitter systems (Dicarlo & Wallace, 2022; Fatemi et al., 2012; Friedman et al., 2006; Karvat & Kimchi, 2014; Xu et al., 2020). These abnormalities help to inform the etiopathogenesis of the motor delays commonly seen in autistic children. Motor learning is a complex neurological task modulated by various neurochemicals (Matur, & Öge, 2017; Leow et al., 2024; Tallet et al., 2015). Motor learning is accompanied by an increase in the cortex of norepinephrine (NE) and acetylcholine (Ach), which primes the system for learning by facilitating alertness and attention (Gold, 2014; Proulx et al., 2014). Then, when the appropriate motor action is approximated, there is a dopamine (DA) release to reward the approximated behavior (Wood, 2021). Finally, new learning is incorporated into memory during sleep (Walker, 2005). Perturbations in these neurochemical processes as well as in sleep function have been identified in the autistic population (Dicarlo & Wallace, 2022; Friedman et al., 2006; Karvat & Kimchi, 2014; Walker, 2005; Yoo et al., 2007).

Precision Intervention: A Unique Opportunity for Occupational Therapy

Precision medicine is an emerging approach in healthcare that seeks to establish patient phenotypes and deliver precise interventions for that phenotype (NIH, 2023). This approach has gained traction in fields such as cancer treatment. The heterogenous nature of autism makes it a particularly relevant target for this type of approach, but it has not yet found a home in the world of autism. (Lombardo et al., 2019; Vicedo, 2023).

The field of occupational therapy is posed to have a unique contribution to precision autism intervention and practices as it relates to motor skill development. Occupational therapy practitioners (OTPs) already consider a wide range of person-specific factors and investigate how these relate to functional performance. Clinicians consider both performance skills and client factors when assessing occupational performance (AOTA, 2020). The next step is to identify interventions based on a better understanding of the underlying biological differences of autistic clients. The future of autism intervention should be grounded in a firm understanding of the client's divergent biological phenotype. In addition, interventions should attempt to enhance neurological processing alongside motor skill training to provide more effective and efficient therapy. This approach to intervention has the potential to impact client factors, performance skills, and, ultimately, occupations (AOTA, 2020).

A potential starting point for addressing this complex problem of precision intervention in motor learning is to create a motor phenotype for autism. Autistic phenotypes have been heavily invested in from the lens of genetics, but the field has yet to produce meaningful, widespread phenotypes to guide treatment (Kalin, 2021; Matta et al., 2022; Nisar et al., 2019). A motor phenotype that links motor performance to biological measures has clinical utility and could potentially provide guidance to clinicians as they choose which intervention approach to utilize for a given client.

In addition, deploying an adjunctive intervention that targets neuromodulation while also providing motor skill training may result in more effective interventions for this population. One such intervention is vagus nerve stimulation (VNS). VNS is a well-established intervention that involves implanting an electrode on the vagus nerve. This invasive procedure has proven effective in managing seizures and chronic depression (Milby et al., 2008). Recently, the Food and Drug Administration (FDA) has approved VNS for improving motor control after a stroke (Dawson et al., 2021; Liu et al., 2022). The vagus nerve is a salient treatment target because it is involved in the neuromodulation of the catecholamines associated with motor learning (Bowles et al., 2022; Keute & Gharabaghi, 2021). However, the invasive procedure of VNS limits its applicability to an otherwise healthy pediatric population.

A relatively newer innovation is the deployment of vagus nerve stimulation through an external, clip-on device called transcutaneous vagus nerve stimulation (tVNS). This innovation has been successfully utilized in a variety of clinical populations to improve motor learning, along with other gains (Badran et al., 2020; Baig et al., 2019; Capone et al., 2017; Koeing et al., 2021; Merchant et al., 2022; Thakker et al., 2020).

To begin the work of developing a precision intervention model for autism, this program proposes three phases. Phase one is a case-control, correlative study investigating the relationship between biometrics and psychometrics. Phase two is single subject feasibility study to test the acceptability of an adjunct intervention utilizing tVNS and motor skill training. Phase three is a randomized controlled trial to investigate the effectiveness of the proposed intervention. The aims of this program include:

(1) To further elucidate the unique neurobiology of autistic children as it relates to motor skill development.

(2) To test the effectiveness of an adjunct intervention targeting neuromodulation and motor skill learning.

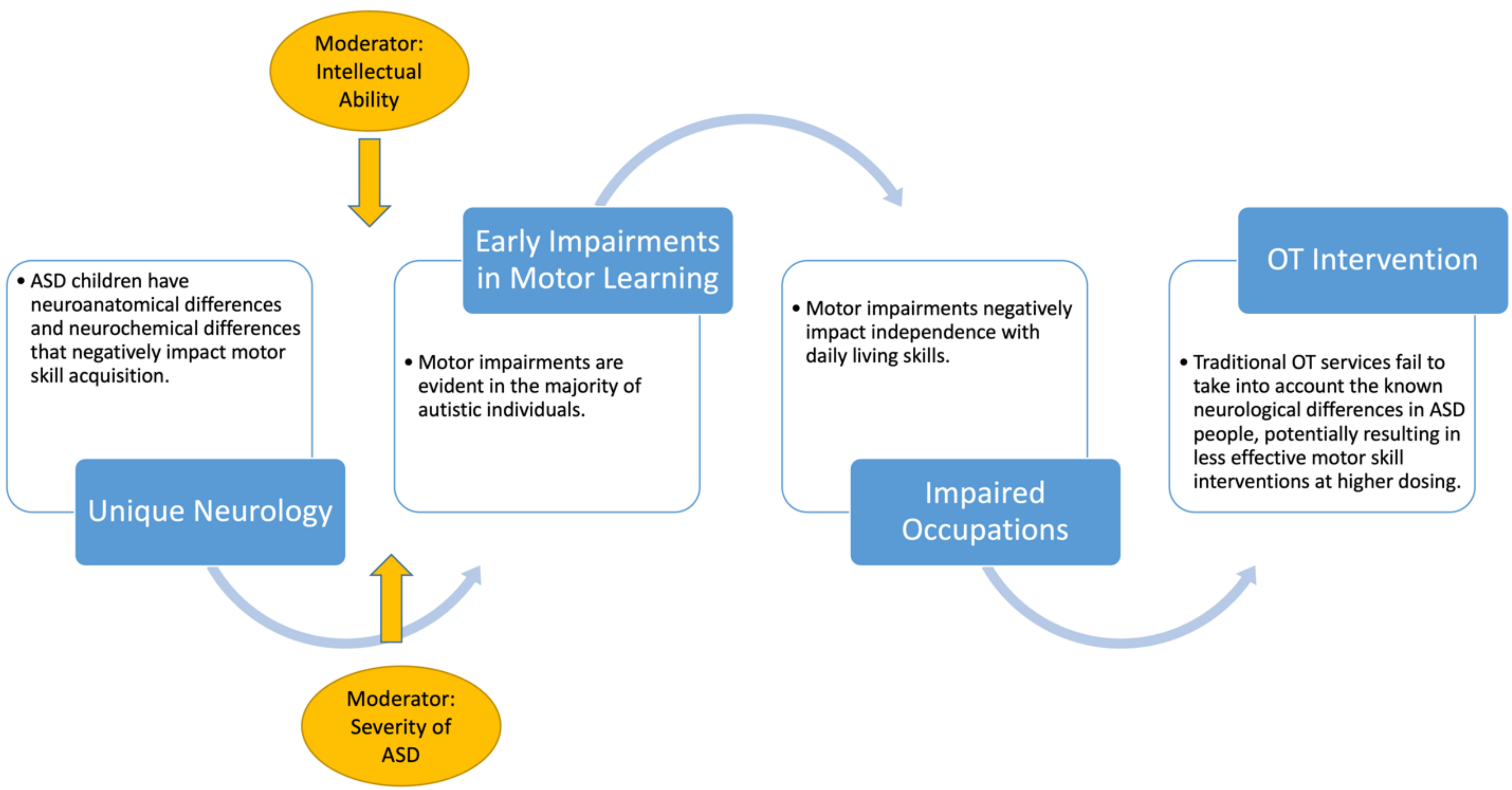
CHAPTER TWO – Project Theoretical and Evidence Base

Overview of the Problem

Autism spectrum disorders are characterized by different social, communicative, and behavioral abilities. Autistic brains have differences in neural architecture, cytoarchitecture, and monoaminergic neurotransmitter systems (Dicarlo & Wallace, 2022; Fatemi et al., 2012; Friedman et al., 2006; Karvat & Kimchi, 2014; Xu et al., 2020). This unique neurology helps to inform the origin of the motor delays commonly seen in autistic children (Bhat, 2020; Kaur et al., 2018). Figure 2.1 details the cascading effects of these differences. Moderators of this pathway include autism severity and intellectual delays. Autistic symptoms vary widely across the spectrum. The severity of symptoms impacts a child's ability to learn new motor actions (MacDonald & Ulrich, 2013). In addition, 37% of people with autism also present with intellectual impairments (CDC, 2024). Intellectual delays negatively impact motor skill development (Jeoung, 2018). Persistent motor skill deficits impact a child's ability to participate in core pediatric occupations, including play, daily living skills, and interacting with others (Dadgar et al., 2017; Kaur et al., 2018; MacDonald & Ulrich, 2013; Ohara et al., 2019; Pan et al., 2017; Travers et al., 2017). This chapter reviews the etiology of motor skill deficits in this population, the theory guiding current motor skill interventions, and how this informs contemporary occupational therapy (OT) practice.

Figure 2.1

Visual Model of Factors Contributing to Less Effective OT Interventions



Occupational therapy and Autism

Occupational therapy practitioners (OTPs) are often part of an autistic child's healthcare team (Benevides et al., 2022). OT research commonly targets a variety of skills including improving social skills, adaptive living skills, feeding skills, problem behaviors, and mental health among other skills (Connor et al., 2022; Kirby et al., 2021; Mazzeo & Caldwell, 2020; Raditha et al., 2023). Despite the widespread occurrence of motor impairments in autistic children, there is a notable scarcity of occupational therapy studies dedicated to enhancing motor skills in this population. Between 2013 and 2023, only 13 experimental, occupational therapy studies included autistic individuals and addressed motor skills (Ajzenman et al., 2013; Alaniz et al., 2017; Alkhalifah et al., 2022; Collins et al., 2015; Hilton et al., 2014; Hirschmann et al., 2023; Iwanga et al., 2014; Jin et al., 2023; Kumar & Nagalakshmi, 2023; Lopez & Kume, 2018; Nuntanee & Daranee, 2019; Schoen et al., 2020; Walsh et al., 2021). This dearth of research despite high rates of motor impairments is surprising. Motor impairments in autistic children are identified at a very young age, even before social and communication delays (Posar & Visconti, 2022). In fact, some explanatory theories assert that social and communication impairments are the sequelae of motor impairments (Ohara et al., 2019; Wilson et al., 2018). As such, motor skills make a salient intervention target.

Current OT intervention varies when addressing motor delays. Researchers have utilized animal-assisted therapy, exercise interventions, aquatic therapy, DIRFloortime, motor skill training, musical rhythm, and sensory integration. Despite the large array of approaches, there is often an absence of key ingredients that support neurological development. This may result in increased intervention dosing to achieve sustainable results. Intervention dosing in the current evidence base ranges from 3–30 hours. Motor acquisition intervention may be more effective if partnered with an adjunct intervention that targets underlying neurological development.

Theoretical Guidance

The lack of OT literature in this content area can be understood through the lens of the publication bias theory as well as the diffusion of innovation theory. These frameworks help to explain why motor skill interventions are underrepresented in occupational therapy literature for autistic individuals.

The publication bias theory suggests that studies with less exciting or eye-catching outcomes tend to have lower chances of being published (Joober et al., 2012). Editors may prioritize research more likely to yield high citation rates (Petrić Howe et al. 2023). Within clinical contexts, targeting improvements in foundational motor skills is a widespread practice in occupational therapy (Tanner et al., 2020). However, research on how occupational therapy specifically enhances motor skills in autistic children might not attract an editor's attention due to a perceived lack of interest. Motor skill interventions may lack the novelty and allure necessary to meet an editor’s criteria for attention-grabbing content. Consequently, this discrepancy might contribute to the scarcity of research supporting motor skill interventions for autistic children within occupational therapy. The publication bias theory sheds light on how the absence of robust research impacts the validation of clinical practices in this domain.

The diffusion of innovations theory provides insights into the difficulty occupational therapy practitioners (OTPs) may have with integrating novel concepts into daily practice. According to this theory, there are several different reasons why a practitioner may choose to incorporate a novel intervention into their practice. A key reason is that the innovation must be considered to be a better alternative to conventional, more familiar practices (Rogers, 2003). Also, the innovation must align with the needs and preferences of the audience expected to embrace these new ideas (NIH, 2012). This theoretical framework helps to explain why OTPs may hesitate to incorporate an intervention that targets underlying biological factors over a more traditional approach. Although there is a large body of research describing these biological differences, studies are predominantly found in fields outside of occupational therapy. In addition, the absence of occupational therapy research investigating adjunct intervention approaches as compared to traditional methods may contribute to the reluctance among OTPs to adopt these innovative ideas.

Review of the Extant Literature

The guiding questions of this search were as follows: (1) Is there evidence of unique neurology in the autistic brain; (2) Is there evidence that autistic children have motor delays at a young age that persist into adulthood; (3) Is there evidence that people with autism present with impairments in occupation that relate to motor skill delays; and (4) Does OT research incorporate key ingredients targeting biological differences when providing intervention to improve motor skills?

Literature Review

A comprehensive search of two databases (PubMed and CINAHL) as well as a search of the American Journal of Occupational Therapy (AJOT) was undertaken using a combination of search terms: autism, autistic, ASD, motor skills, motor acquisition, motor outcome, motor intervention, occupational therapy, activities of daily living, daily living skills, autonomic nervous system, cortex, and neurotransmitter. Limits were set for date, language, and type of publication. In the present review, studies were included for question (1) if a portion of the subjects were identified as autistic AND motor skills were discussed. Studies were included for question (2) if a portion of the subjects were identified as autistic AND neurological function was discussed. Studies were included for question (3) if a portion of the subjects were identified as autistic AND daily living skills were discussed. Studies were included for question (4) if a portion of the subjects were identified as autistic AND occupational therapy AND motor intervention were addressed.

Criteria for exclusion included: a) a publication date that was greater than ten years from present, 2) an article that was in a language other than English, 3) an article that was not published in a peer-reviewed journal (questions one – three), or 4) intervention studies did not include a motor outcome measure (question four). Due to the small amount of OT intervention studies located, poster presentation and conference proceedings published in The American Journal of Occupational Therapy were accepted for review as well. 1,692 articles were identified by the author for review and 32 were selected for critical appraisal.

Five studies were reviewed that detailed motor skill acquisition patterns for people with autism (Kaur et al., 2018; Lidstone & Mostofsky, 2021; Linke et al., 2020; Posar & Visconti, 2022; Tse et al., 2022). Studies investigating autistic neurology comprised of five of the articles reviewed (Bharath et al., 2019; Dadalko & Travers, 2018; Fetit et al., 2021; Kuo & Liu, 2022; Matsushima et al., 2016). Six of the studies included reported on daily living skills related to motor skills in autistic people (Fisher et al., 2018; Kruger et al., 2019; Ozboke et al., 2021; Travers et al., 2017; Travers et al., 2022; Volkan-Yazici et al., 2018). All thirteen papers that were identified investigating the use of occupational therapy to improve motor skills in autistic children were reviewed (Ajzenman et al., 2013; Alaniz et al., 2017; Alkhalifah et al., 2022; Collins et al., 2015; Hilton et al., 2014; Hirschmann et al., 2023; Iwanga et al., 2014; Jin et al., 2023; Kumar & Nagalakshmi, 2023; Lopez & Kume, 2018; Nuntanee & Daranee, 2019; Schoen et al., 2020; Walsh et al., 2021). In addition, three review studies on this topic were included (Bagatell & Mason, 2015; Friedman et al., 2023; Schaaf et al., 2018).

Autistic Neurology. Five studies were chosen for this review (Bharath et al., 2019; Dadalko & Travers, 2018; Fetit et al., 2021; Kuo & Liu, 2022; Matsushima et al., 2016). Two were case control studies (Bharath et al., 2019; Matsushima et al., 2016) and three studies were reviews (Dadalko & Travers, 2018; Fetit et al., 2021; Kuo & Liu, 2022). Findings revealed idiosyncratic neurology in autistic individuals. Differences were found in the cytoarchitecture and neurotransmitter systems but these findings were not consistent from person to person or from one age level to another. Cytoarchitecture differences included abnormal brain growth, abnormal neuronal density, poor myelination and excess dendritic spines (Dadalko & Travers, 2018; Fetit et al., 2021). Neurotransmitter differences included GABAergic dysfunction, glutamatergic dysfunction, and abnormal catecholamine levels (Bharath et al., 2019; Fetit at al., 2021; Kuo & Liu, 2022).

Of particular interest, vagal nerve tone was found to be decreased in autistic individuals when compared to neurotypical peers (Matsushima et al., 2016). Vagal nerve tone is commonly measured indirectly via heart rate variability (HRV). HRV is one measure of autonomic nervous system functioning (Dadalko & Travers, 2018; Matsushima et al., 2016). Lower HRV has been described in autistic individuals (Bharath et al., 2019). These are relevant findings as the vagus nerve influences several neurotransmitters, including dopamine and norepinephrine, and these monoamines are consistently found to be poorly regulated in autistic individuals (Kuo & Liu, 2022). They also serve an important role in motor learning and motor skill achievement.

A strength of these studies was the well-described methodologies. However, methodologies varied from study to study. Also, several of the studies were comprehensive reviews, but the population was not always thoroughly characterized nor was there a statistical analysis to determine if the sample sizes were sufficient. Despite these weaknesses, the research illuminates important information about the autistic brain.

Motor Skills in Autism. Data extraction for these studies focused on conceptualizing motor development over time in people with autism. Five studies were reviewed. Demographics ranged from birth to adulthood and included the full spectrum of severity of autism. One of the studies was a systematic review (Tse et al., 2022); two of the studies were narrative reviews (Lidstone & Mostofsky, 2021; Posar & Visconti, 2022) while two were case-control studies (Kaur et al., 2018; Linke et al., 2020). Findings indicate motor delays can be observed as young as six months old and remain present into adulthood (Linke et al., 2020; Posar & Visconti, 2022; Tse et al., 2022). In addition, the severity of motor delays is predictive of autism symptom severity, social skills, and language skills (Kaur et al., 2018; Lidstone & Mostofsky, 2021; Posar & Visconti, 2022).

The strength of these studies was the consistency in findings from study to study. The weakness was a poorly characterized population. Studies failed to include information regarding socioeconomic status, race, and geographical location which weakens the studies' applicability.

Occupational Impairment. Six studies were reviewed that assessed the correlation between motor skills and daily living skills. Demographics ranged from four to 40 years old. Of the studies reviewed, three were cross-sectional studies (Fisher et al., 2018; Kruger et al., 2019; Travers et al., 2022), one was a correlative study (Ozboke et al., 2021), one was a case-control study (Volkan-Yazici et al., 2018), and one was a longitudinal study (Travers et al., 2017). Similarities were found in all studies, indicating that motor skills predict daily living scores. The severity of autistic symptoms negatively correlated with both motor skills and functional living skills (Kruger et al., 2019; Ozboke et al., 2021). The strengths of these studies included sufficient sample sizes and valid outcome measures. The primary weakness of these studies is a lack of consensus on appropriate outcome measures.

Motor Skills Intervention in Children with Autism. Data extraction for these studies focused on identifying the guiding theory, proposed mechanism of action, and key ingredients of the interventions to determine if current OT practice addresses biological differences in autism when designing the intervention. Three of the studies were reviews (Bagatell & Mason, 2015; Friedman et al., 2023; Schaaf et al., 2018), two were randomized controlled trials (Hirschman et al., 2023; Jin et al., 2023), one was a single subject study (Alkhalifah et al., 2022), two were repeat measures (Alaniz et al., 2017; Hilton et al., 2014), three were quasi-experimental (Ajzenman et al., 2013; Kumar & Nagalakshmi, 2023; Nuntanee & Daranee, 2019), three were poster presentations (Collins et al., 2015; Lopez & Kume, 2018; Walsh et al., 2021), one was a research platform presentation (Schoen et al., 2020), and one was retrospective (Iwanga et al., 2014).

Review studies demonstrated agreement in intervention effectiveness (Bagatell & Mason, 2015; Friedman et al., 2023; Schaaf et al., 2018). The outcome measures utilized varied from study to study and were often non-standardized or proxy measures. Evidence was generally low quality with small sample sizes and limited randomized controlled trials.

Demographics from the intervention studies included children ages 2–19 years old. Intervention types varied widely and included sensory integration (Alkhalifah et al., 2022; Schaaf et al., 2018), DIRFloortime (Hirschmann et al., 2023), exercise/ strengthening (Hilton et al., 2014; Lopez & Kume, 2018; Kumar & Nagalakshmi, 2023; Schoen et al., 2020), animal-assisted therapy (Ajzenman et al., 2013; Nuntanee & Daranee, 2019), aquatics (Alaniz et al., 2017; Walsh et al., 2021), targeted skill interventions (Jin et al., 2023) and music-based interventions (Friedman et al., 2023). Intervention dosage also varied widely ranging from three hours to 24 hours with an average of 12.7 hours of intervention. The frequency of intervention also had a wide scope, ranging from one session weekly to three sessions weekly. Duration of sessions ranged from 3 minutes to 90 minutes per session. Outcome measures also varied widely with 13 different motor measures used across 13 studies. The Bruininks-Oseretsky Test of Motor Proficiency (BOT) was the most frequently cited measure occurring in three studies. There is no consensus in the literature for an appropriate battery of outcome measures for the autistic population.

A noticeable weakness of these studies is the small sample sizes. All studies combined (excluding reviews) included a total of only 161 autistic subjects. In addition, the large majority of motor skill intervention studies do not explicitly state a theory base. However, studies implicitly suggest the use of motor learning theory, applied behavior analysis theory, neuroplasticity theory and/or sensory integration as the guiding theories for intervention design. Motor learning theory focuses on feedback and practice schedules (Levin & Demers, 2021). Applied behavior analysis focuses on operant conditioning and positive reinforcement (Madden et al., 2023; Felzer-Kim & Hauck, 2020). Neuroplasticity and sensory integration both emphasize the ability to make neurological changes as an adaptive response to experiences (Pfeiffer et al., 2011; Shaffer, 2016). Clearly identifying a theory base, proposed mechanism of action and key ingredients is necessary to improve the evidence base. An additional weakness of this study set is the low level of research quality. Only two randomized controlled trials were identified. Fidelity to intervention was measured in only two studies, discussed in one, and not addressed at all in ten of the intervention studies. Strengths in these studies included appropriate inclusion and exclusion criteria and appropriate application of statistics.

There is overall a deficiency of research investigating the impact of occupational therapy on motor skills in autistic children. Although some of the studies acknowledged neuroplasticity as a mechanism of action, none of the research considered the specific neuroanatomical differences of autistic brains.

Conclusion

The prevalence and impact of motor skill deficits in autistic children are widely acknowledged. These deficits impact occupational performance. However, the current evidence base in occupational therapy for guiding motor skill interventions is shallow. Also, despite the known neurological differences in autistic individuals, adjunct interventions targeting these differences are notably absent in the occupational therapy research. Theoretical frameworks such as publication bias and diffusion of innovations theories help explain the gaps between research and practice. This review of the literature emphasizes the need for more rigorous studies addressing motor skill interventions informed by neurological differences in autistic individuals. Studies reviewed indicate a wide range of intervention approaches, dosing, and frequency of intervention. The studies included in this synthesis had clearly stated aims that were aligned with the PICO (Population, Intervention, Comparison, Outcome) framework guiding the literature search. Inclusion criteria were appropriate across studies and outcome measures were appropriate and of high quality. However, the quality of the studies was generally low. This was primarily due to the limited number of randomized controlled trials, poorly characterized populations, and the inclusion of small sample sizes. This diminishes the generalizability and statistical power of the findings.

When taken together, these studies suggest that an adjunct intervention targeting neuroplasticity, combined with a motor intervention that includes positive reinforcement and explicit feedback and practice schedules may be beneficial for amplifying gains in motor skill training.

CHAPTER THREE – Overview of Current Approaches and Methods

Overview

Autism impacts one out of every 36 children and is characterized by a range of challenges, including motor skill deficits (CDC, 2023). In recent years, there has been growing interest in developing effective interventions to address motor skills. Because the occupational therapy (OT) literature is so sparse, intervention in related fields must be considered. One promising approach to treatment involves transcutaneous vagus nerve stimulation (tVNS) as an adjunct to traditional motor skill training. By combining tVNS with motor skill training, researchers aim to achieve better outcomes with smaller doses of intervention. This chapter provides an overview of the current literature in related fields on motor skill interventions for individuals with autism. In addition, it reviews the literature on the emerging use of tVNS as an adjunct therapy for motor skill acquisition.

Literature Search

A comprehensive search of three databases (PubMed, CINAHL, and APA PsycINFO) was undertaken using a combination of search terms: autism, autistic, ASD, motor acquisition, motor intervention, effectiveness, tVNS, and VNS. Limits were set for date, language, and type of publication. Studies were included if: a) a portion of the subjects were identified as autistic, AND b) motor skill intervention was deployed, AND/OR c) tVNS/ VNS/ vagal nerve function were addressed. Criteria for exclusion included: a) a publication date that was greater than ten years from present, 2) an article that was in a language other than English, or 3) an article that was not published in a peer-reviewed journal. The guiding questions of this search were as follows:

(1) Outside the field of OT, what is the current state of the literature describing motor intervention in children with autism?

(2) For autistic children with motor skill deficits, does the use of tVNS paired with motor skill training improve skill acquisition?

101 articles were identified by the author for review, and ten were identified for critical appraisal. Five reviews reported on the effectiveness of motor skill intervention in children with autism (Cameron et al., 2020; Case & Yun, 2019; Ceccarelli et al., 2020; Huang et al., 2020; Ruggeri et al., 2020). Five of the studies explored the use of vagus nerve stimulation (VNS) or transcutaneous vagus nerve stimulation (tVNS) in autistic individuals (Engineer et al., 2017; Holland & Manning, 2022; Jin & Kong, 2016; Matsuchima et al., 2016; Van Hoorn et al., 2019). The results of the search are summarized below.

Motor Skills Intervention in Children with Autism

Outside of the field of OT, a considerable body of research has focused on investigating the efficacy of motor skill interventions for children with autism. These interventions encompass a variety of approaches. The following section provides an overview of the current evidence regarding motor skill interventions for autistic children, highlighting key studies and their findings.

Interventionists. A range of disciplines address motor skill development in autistic children. Common interventionists include behavioral analysts, physical therapists, and physical education instructors (Cameron et al., 2020; Case & Yun, 2019 Ceccarelli et al., 2020). As described in chapter two, OT is less commonly represented in the motor skill intervention literature. Overall, there is no consensus on what type of interventionist is most effective for improving motor skills in autistic children.

Types of Motor Skill Interventions. Fundamental motor skills are, “The essential movements that allow a person to successfully perform a variety of physical activities — such as walking, running, jumping, reaching, catching and throwing” (Ceccarelli et al., 2020, p.2). In the motor skill literature, fundamental motor skills are the most common target of intervention. Intervention approaches vary widely, reflecting the diversity of strategies utilized to address motor skill deficits in autistic children. Examples include specific motor skill training programs, sports-based interventions, technology-based interventions, aquatics, and equine-related interventions (Borgi et al., 2016; Caputo et al., 2018; Najafabadi et al., 2018; Rafie et al., 2017; Toscano et al., 2018). Again, we find that there is no agreement on the most effective approach for addressing motor skill acquisition in this population. In addition, a theory base is rarely stated.

Dosing of Motor Skill Interventions. The frequency of intervention also varied widely, ranging from 1 session weekly to 5 sessions weekly (Guest et al., 2017; Cei et al., 2017). The duration of sessions ranged from 15 minutes to 90 minutes (Dickinson & Place, 2014; Huang et al., 2020). Minimum dosing for effectiveness was identified at 16 hours of intervention (Case & Yun, 2019) and was commonly seen at 36 hours or more (Huang et al., 2020; Ruggeri et al., 2020).

Strengths and Limitations of Current Motor Skills Intervention Studies

There is widespread interest across disciplines in improving motor skills in children with autism. This interest is reflected in the great plethora of intervention types. When motor intervention studies are viewed together, results are consistent from study to study. Interventions have a positive impact on motor skill acquisition. However, the quality of the studies is generally low. This is primarily due to the limited number of randomized controlled trials and the inclusion of small sample sizes.

Another notable gap in motor intervention studies is the frequent omission of the theoretical frameworks used to inform intervention design. The lack of a theory base limits the understanding of the causal pathway guiding the development of the intervention. It also limits the potential for replicability and refinement of the theory base. Also, the studies reviewed most-commonly-measured body functions and structures but did not consistently measure participation outcomes. This limits the comprehensive understanding of the impact of the intervention on occupational performance.

VNS Interventions

In addition to traditional motor skill training, adjunct therapies targeting vagal tone were also analyzed.

Background. The vagus nerve (cranial nerve X) originates in the brainstem and stretches all the way to the colon. As such, it is the longest cranial nerve in the body (Kenny & Bordoni, 2019). It has both afferent and efferent projections that provide information back and forth between the body and the brain. The vagus nerve is 80%

afferent fibers, conveying somatic information (information from the body) to the brainstem (nucleus tractus solitaries and the spinal nucleus of the trigeminal nerve) which then indirectly projects to a variety of cortical brain regions including the locus coeruleus, hippocampus, and amygdala (Yamakawa et al., 2015). As such, the vagus nerve has widespread influence over many cortical functions. Although the role of the vagus nerve is not fully known, studies suggest that it has an impact on neuromodulation (Howland, 2014).

Vagus nerve stimulation (VNS) is an invasive procedure that involves implanting a device on the left cervical branch of the vagus nerve (Engineer et al., 2017). It has been proven effective in managing a wide range of disorders including seizures, migraines, tinnitus, and depression (Austelle et al., 2022; Jain & Arya, 2021; Song et al., 2023; Stegeman et al., 2021). More recently, it has been utilized as an adjunct to stroke rehabilitation (Liu et al., 2022). Transcutaneous vagus nerve stimulation (tVNS) is a relatively new, noninvasive intervention that targets the afferent fibers of the vagus nerve. The vagus nerve passes to the cutaneous level at the ear and can be stimulated using a clip-on device. Transcutaneous vagus nerve stimulation has a less developed research base, but is thought to work in similar ways as VNS.

Mechanism of Action. The proposed mechanism of action VNS/tVNS is multi-fold and includes reducing inflammation, increasing neuroplasticity, and improving arousal modulation.

Reduces Inflammation. Researchers believe that VNS reduces inflammation in the body and the brain (Bonaz, 2022). Peripheral inflammation is thought to be influenced via the cholinergic anti-inflammatory pathway (de Jonge et al., 2005). In the brain, the vagus nerve improves the blood-brain barrier which in turn reduces inflammation (Lopez et al., 2012).

Increases Neuroplasticity. Neuroplasticity is mediated by the release of certain neurotransmitters. The vagus nerve is thought to have a modulating effect on acetylcholine and the catecholamines norepinephrine and dopamine (Manta et al., 2013; Radet et al., 2011). As previously discussed, these neurotransmitters are involved in new motor learning. In addition, VNS appears to improve the expression of brain derived neurotrophic factor (BDNF) (Rosso et al., 2020). BDNF is a neuromodulator that influences plasticity in the hippocampus (Camuso et al., 2022). The hippocampus has a primary role in spatial learning, contextual learning and memory consolidation (Cherry, 2022).

Improves Arousal Modulation. VNS may influence the GABAergic system which is an inhibitory network. It plays a large role in regulating neuronal excitability (Schmidt-Wilcke et al., 2018). GABA also plays a role in sleep (Gottesmann, 2002). GABA has been shown to increase significantly after VNS stimulation (Keute et al., 2018).

Adjunct Therapy and Motor Skill Interventions

The extant literature was reviewed to determine how tVNS is being applied in clinical research. The following section provides an overview of the current evidence regarding tVNS interventions, highlighting key studies and their findings.

Interventionist. Studies on the effectiveness of tVNS vary widely. Most studies do not reveal the qualifications of the interventionist. Capone et al. (2017) had physical therapists and physicians supervising the intervention. Comparatively, parents implemented an at-home intervention in Merchant et al. (2022). However, the majority of studies fail to disclose the qualifications of the person delivering the intervention.

Types and Dosing of Adjunct Motor Skill Interventions. Intervention targets for tVNS varies greatly and spans from stroke rehabilitation to mental health improvement to language development (Capone et al., 2017; Koeing et al., 2021; Thakker et al., 2020). Studies utilize a variety of devices to provide stimulation. Across all studies, the device targets the auricular branch of the vagus nerve. Settings of the tVNS device vary in both intensity and duration. Stimulation during each treatment session ranges from five minutes to sixty minutes (Capone et al., 2017; Merchant et al., 2022).

Very few studies have been completed in pediatrics using tVNS. Badran et al., (2020) investigated the impact of tVNS on neonates to improve feeding skills. They were able to establish the safety of tVNS stimulation in newborns as well as demonstrate gains in feeding. In similar fashion, Merchant et al. (2022) demonstrated the safety using tVNS to address kidney disease in children while obtaining clinical remission. These studies suggest that tVNS may be a safe and effective intervention tool for addressing a wide range of diagnoses in pediatrics.

When taken together, these findings suggest that vagus nerve stimulation enhances plasticity through a priming of the neural environment to create a milieu conducive to motor learning. Reduced vagal tone has been noted in autism (Klusek et al., 2013; Matsushima et al., 2016; van Hoorn et al., 2019), making it a salient intervention target as an adjunct to motor skill training.

Quality and Limitations of Current tVNS Research

Although promising, the tVNS literature addressing motor skills is in its infancy. There is variation among populations and targeted outcomes in the evidence base. The most well-established outcome in the VNS literature is in reducing seizures (Englot et al., 2011; Fukuda et al., 2024). Newer studies are laying the groundwork for utilizing vagus nerve stimulation in motor rehabilitation (Dawson et al., 2021). There is even less evidence on the use of tVNS in the clinical population. However, evidence in rehabilitation is emerging. The mechanism of action is not fully understood, but studies suggest that the vagus nerve supports neuroplasticity. As tVNS is established as safe for the pediatric population, calls for investigating its impact on autism are mounting (Engineer et al., 2017; Holland & Manning, 2022; Jin & Kong, 2016; Zhu et al., 2022).

Conclusion

Children with autism commonly present with motor skill deficits (Green et al., 2009; Lidstone & Mostofsky, 2021). The etiology of these deficits is not clearly established. Differences in both motor skill acquisition as well as motor movement patterns have been observed (Posar & Visconti, 2022). Although intervention can improve these skills, there is not a consensus on what the key ingredients are required in an effective intervention approach (Case & Yun, 2019). Vagus nerve stimulation technology recently received Food and Drug Administration (FDA) approval for use in motor skill recovery in stroke patients. The proposed mechanism of change is via neuroplasticity as a result of cholinergic and noradrenergic neuromodulatory systems (Engineer et al., 2017; Jin & Kong, 2016; van Hoorn et al., 2019). It has proven to be a safe intervention with relatively few and minor complications (Jin & Kong, 2016). The application of this technology in the pediatric population is limited. However, it is promising as an adjunctive therapy to improve motor skills in children with autism (Engineer et al., 2017). There is a verdant landscape for future research direction on this topic. The field of occupational therapy is poised to pioneer innovative interventions in this area of development.

CHAPTER FOUR – Description of the Proposed Program

Overview

This OTD project is a three-phase study design investigating the impact of a biological adjunct intervention on motor skill acquisition in autistic children. The first phase focuses on examining biometrics and their psychomotor implications in individuals with autism. This phase serves as a formative evaluation to inform the intervention phases. The second phase is a feasibility study that investigates the viability of implementing an intervention that targets both biological and physical factors. Finally, the third phase is a large-scale, randomized controlled trial that builds on the feasibility study's findings.

Phase One

Autistic brains have known differences when compared to neurotypical samples. Autistic neurology has been studied in many different formats including postmortem histology studies, plasma and urine studies, and imaging studies to name a few. A large portion of the literature has been conducted on animal models (Kuo & Liu, 2022). This is, in part, due to the difficulty of obtaining biological samples from live, healthy subjects. Procedures for assessing neurological function can be difficult for subjects to tolerate. Phase one of this project attempts to identify and trial non-invasive measures of neurobiological functions in autistic children. In addition, psychomotor measures will be gathered to characterize motor skill functioning and its impact on daily living skills. Finally, data will be analyzed for correlations between neurobiological functions and psychomotor measures. By generating this data, a clearer picture of the unique neurology of autism and how this relates to physical skills will emerge. This allows the identification of motor phenotypes for more targeted intervention, which leads to phase two.

Phases Two and Three

Phase two is a feasibility study that investigates implementing an adjunct intervention targeting biological factors while also providing occupational therapy targeting physical factors. This feasibility study will be a small-scale, single-subject design investigating the acceptability of the planned intervention. The intervention will include transcutaneous vagus nerve stimulation (tVNS) which is a non-intrusive device that clips to the ear lobe and provides stimulation to the vagus nerve as it passes close to the skin surface. This stimulation will be paired with motor skill training. Finally, the feasibility study will inform a large-scale randomized controlled trial (RCT), which is phase three of this project.

Theory of Change and Explanatory Model

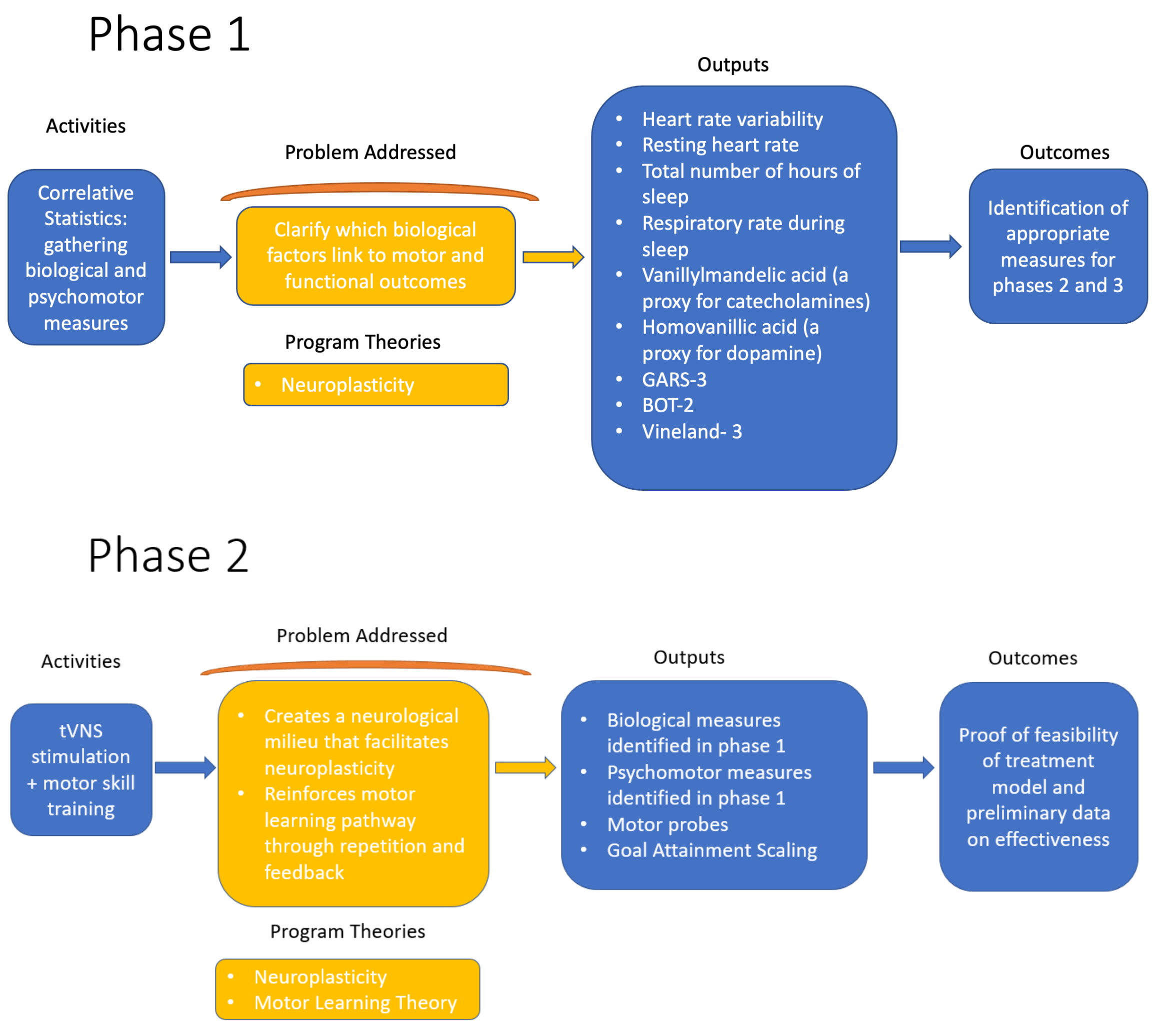
The first hypothesized mechanism of action is based on motor learning theory which is centered on providing feedback on a given practice schedule (Jarus & Gutman, 2001). Motor learning theory suggests that by engaging in repetitive motor tasks and receiving different types of feedback, the cortex undergoes reorganization (Winstein et al., 2014). As individuals repeatedly perform motor tasks, the brain forms new neural pathways and strengthens existing connections in the cortex (Jessell et al., 2011). This process of cortical reorganization allows for the development of more efficient motor control and improved performance of the task (Franklin & Wolpert, 2011). Additionally, receiving intrinsic and extrinsic feedback during the practice of these tasks provides information to the cortex about which movements are successful and which ones need to be adjusted (Aoyagi et al., 2019).

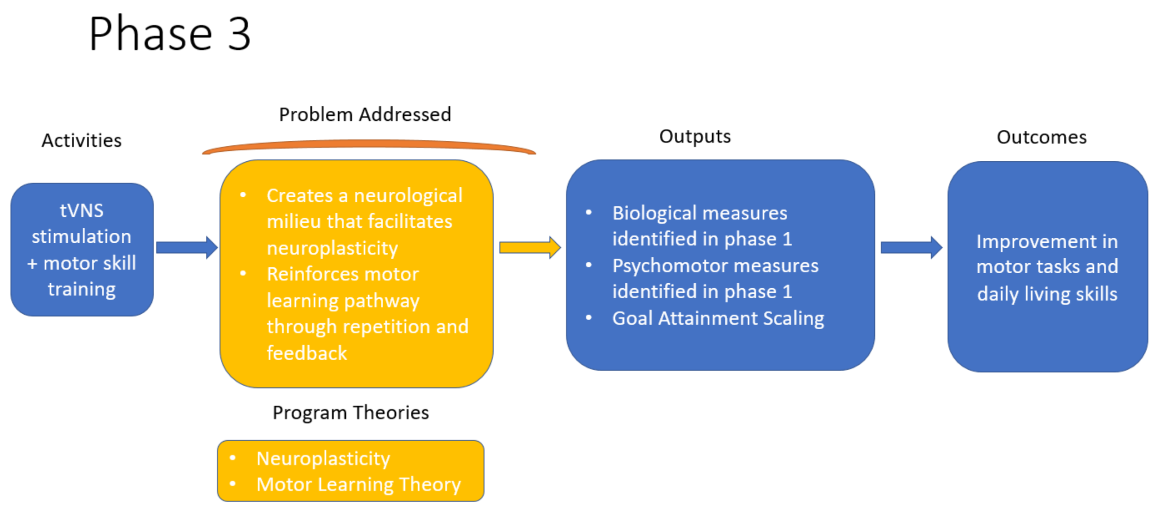
The second mechanism of action is based on neuroplasticity. Vagus nerve stimulation may be effective for improving neuromodulation in this population by targeting the catecholamines of dopamine, norepinephrine, and epinephrine (Kuo & Liu, 2022). These neurotransmitters have been implicated in the etiology of autism and have a major role in motor skill development (DiCarlo & Wallace, 2022; Friedman et al., 2006; Karvat & Kimchi, 2014; Yoo et al., 2007). Vagal nerve tone is established as low in people with autism and in turn, this may negatively impact motor learning (Engineer et al., 2017; Matsushima et al., 2016). A promising development in intervention is pairing tVNS with motor skill training to achieve better outcomes with potentially smaller dosing of intervention (Dawson et al., 2021; Li et al., 2022; Liu et al., 2022; Morrison et al., 2019). By enhancing vagal nerve tone, neuroplasticity is increased, and this in turn can improve motor skill acquisition (Dadalko & Travers, 2018).

In this three-phase project, each phase builds on the next. Figure 4.1 details the explanatory model for each phase.

Figure 4.1

Explanatory Model for Phase One (Correlative Study), Phase Two (Single Subject Design), and Phase Three (Randomized Controlled Trial)





Note: Gilliam Autism Rating Scales, third edition (GARS-3); Bruininks-Oseretsky Test of Motor Proficiency, second edition (BOT-2); Vineland Adaptive Behavior Scales, third edition (Vineland-3)

Stakeholders

Engaging key stakeholders in development and implementation is an important part of research. Establishing a connection early on, listening to a diverse group of perspectives, and opening the research process up to critical feedback helps to refine the design of the program. In this program, stakeholders are categorized into micro, meso, and macro-levels. At the micro-level, research participants and their families are key stakeholders who will be involved in both the formative and summative evaluation processes. At the meso-level, there are several important stakeholders. The primary investigator is involved in each phase of the research. The primary investigator ensures that the implementation of the program maintains fidelity to the planned design. Also, the primary investigator works to develop manuscripts for publication. The hospital where the research takes place and the director of research within that institution are also meso-level stakeholders. These stakeholders provide the context and infrastructure for implementing the research. They also offer feedback on the research design. Their focus is on ensuring successful outcomes for the patients involved, as well as facilitating the production of high-quality research.

At the macro-level, stakeholders include professional organizations and medical insurance regulators. Professional organizations such as the American Occupational Therapy Association serve the role of knowledge dissemination to ensure the research findings are made available to practitioners. Also, findings from each phase can be utilized for advocacy efforts by organizations such as the American Occupational Therapy Political Action Committee, potentially influencing policy changes regarding the use and reimbursement of innovative interventions. These policy changes can significantly contribute to the widespread adoption of such adjunctive practices across the field of occupational therapy.

Program Scenario

Participants will be autistic children aged 8–8 years 11 months old and their families. A case scenario is provided in Figure 4.2

Figure 4.2

Illustrative Program Practice Scenario

Jessica is the mother of a child with autism with motor skill deficits. Despite receiving occupational therapy (OT), her son was not responding to intervention and the authorized insurance visits were running out. She talked to her occupational therapy practitioner (OTP) about adjusting the intervention approach to try to obtain faster gains for her son. Her OTP proposed an experimental approach, utilizing transcutaneous vagus nerve stimulation (tVNS) to facilitate neuroplasticity during the OT sessions. Jessica and her son agreed to the experiment and after just 8 sessions, her son achieved his goals. As his motor skills continued to improve with additional sessions, her son was able to achieve independence with many of his daily living skills. These gains were all obtained before insurance benefits ran out. Jessica was thankful for an efficient an effective intervention and was hopeful that the changes established during this course of treatment would have a longstanding impact on her son's motor development.

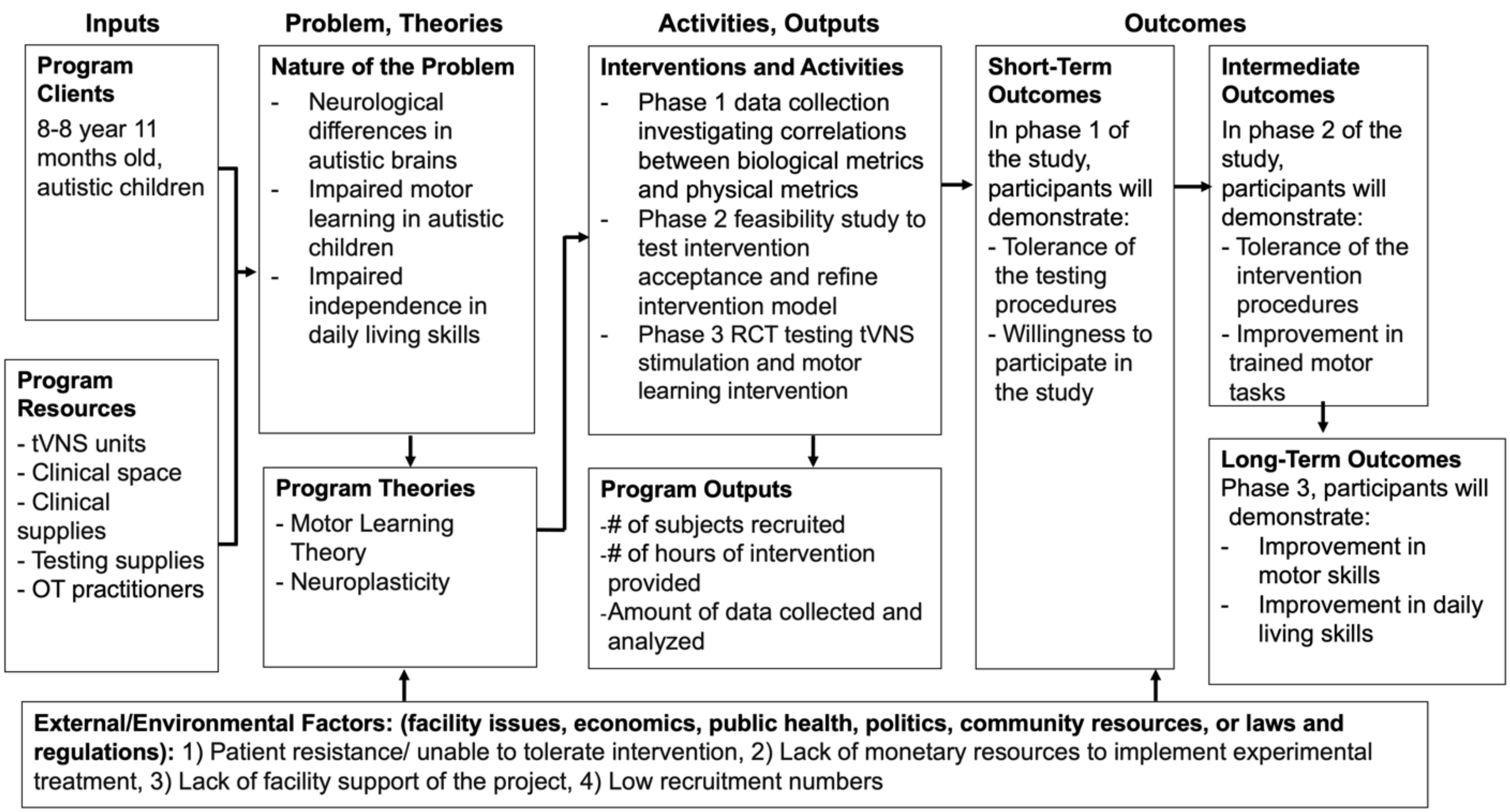
Objectives

The objectives of this program include: (1) identify salient biological patterns related to motor and functional outcomes (motor skills phenotypes); (2) increase motor skill acquisition with decreased dosing; and (2) increase independence with daily living skills. Figure 4.3 illustrates the key elements of the entire program. The goals of all three phases collectively are to illuminate the neurobiological intricacies of autism, and provide more precise and effective interventions for this diverse population.

Figure 4.3

Full Logic Model

Program title: ***Innovative Interventions: Neuromodulation to Enhance Motor Learning***



Personnel

The people responsible for the delivery of this program will be OTPs in an outpatient pediatric clinic. The primary investigator will supervise the training and implementation of the intervention. Evaluators and interventionists will be trained prior to the start of the project to ensure competency. Training will include synchronous and asynchronous activities, practice sessions, and return demonstrations to ensure competency. Please refer to Appendix A for an example of a teaching plan to be utilized in the training. An intervention manual will be created that details the feedback and repetition schedule. Weekly team meetings will be held to review intervention sessions and clarify any questions. Finally, all intervention sessions will be videotaped and 10% of sessions will be randomly reviewed and rated for fidelity. Any sessions rated below the set threshold will trigger additional coaching and supervision for that interventionist.

Participants and Location

Children between the ages of 8 years and 8 years 11 months old are the targeted population for this program. Phase one will include both neurotypical and autistic children whereas phases two and three will include only autistic children. All testing and intervention will be completed at the Children's Services Center on the Casa Colina Pomona campus. Phase one will require one to two visits for data collection. Phases two and three will require baseline testing, 24 hours of intervention, and endpoint testing.

Planned Outreach

Plan to Involve Key Stakeholders in the Evaluation Process

In order to involve stakeholders from the beginning of the program through the completion, meetings will be set in both virtual and in-person settings. This will allow for flexibility and accessibility. Stakeholders will be provided with information about the program, including the fact sheet and executive summary documents, which are found in the appendices of this paper. The logic model will also be shared to ensure that a comprehensive understanding of the program is obtained. Stakeholders will include the Director of Research, potential program participants' families, and program staff. Discussions will be structured to facilitate stakeholder input on research questions, design elements, and insights on how the evaluation findings will be utilized.

Study Type

Phase one is a case-control, correlative study of two groups of children between the ages of 8 years and 8 years 11 months old. One group will be composed of neurotypical children to serve as the control group. The second group will be composed of age and sex-matched autistic children. Phase two is a single-subject design study to test intervention feasibility. Intervention pairing tVNS with motor skill learning will be trialed with a small group of subjects and measurements will be collected after six hours, 12 hours, 18 hours and 24 hours of intervention. Finally, phase three is a randomized controlled trial designed to establish causality. Subjects will be randomly assigned to an intervention or a wait list control group. Evaluators will be blinded to group assignment and intervention will be implemented by clinicians who are trained in the manualized intervention. Fidelity checks will be implemented throughout the intervention process.

Methods

Intervention Delivery, Activities and Flow

Phase one involves testing procedures only. Psychomotor testing will be provided by trained and licensed occupational therapists following standardized procedures that are described in the outcome measures' manuals. Parents will receive face to face instruction on the use of the wearable device for gathering biometric data. They will also receive a written protocol for their reference. Biometric data gathered during sleep will be conducted over a two-week timeframe. Laboratory biometric data will be collected and processed at a third-party location that has established proficiency and accuracy with administering identified tests. Phase two involves collecting qualitative data via parent and clinician surveys. Surveys will be implemented by the primary investigator face to face with the stakeholders and will follow a pre-set list of questions.

Phases two and three involve intervention procedures. Intervention will be provided by trained and licensed occupational therapists and will follow a manualized program. Once baseline testing is completed, participants will be seen twice a week for sessions that are 50 minutes in duration. Intervention sessions will include tVNS stimulation for 20 minutes following parameters established by previous research (Jin & Kong, 2016; Li et al., 2022). The stimulation parameters will be set at 0.3-ms square pulses at 20 Hz for 30 seconds repeated every 5 minutes for a total of 20 minutes. The stimulation will immediately be followed by 30 minutes of traditional motor skill training following a manualized procedure. Fidelity checks will be utilized to ensure intervention follows the manualized procedures. Intervention sessions will be videotaped and 10% will be randomly chosen for video review to ensure fidelity. Videos will be taken utilizing clinic iPads and data and videos will be stored in our Health Insurance Portability and Accountability Act (HIPPA) protected computer system. Statistical data software will be utilized to analyze the data.

Controls

Threats to Internal Validity

In order to limit confounding factors contaminating the study findings, several strategies will be utilized. To limit attrition bias, subjects will be financially incentivized. Selection bias is also a threat for this study. Although convenience sampling will be utilized for phase two (feasibility study), phase three will attempt to expand the sampling to a larger geographical location. The selection of controls for phase one will include careful age and sex-matching. Finally, clear inclusion and exclusion criteria will be established to limit selection bias. Instrumentation will be addressed by ensuring proper training in administering the standardized assessments, including spot-checks for adherence.

Potential Sources of Bias

Performance bias is possible if there is a deviation from the intervention protocol. To mitigate this bias, a manualized intervention will be developed. However, performance bias is still possible in this study. Usual care will be allowed to continue which could contaminate the subject pool. In addition, this is not a double-blinded study. Participants and interventionists will be aware of group allocation. Detection bias will be limited by blinding the outcome assessors. Reporting bias will be addressed by publishing the intent of the randomized controlled trial on www.clinicaltrials.gov prior to the implementation of the study.

Program Outputs and Outcomes

Outputs for all three phases include biometric data and psychometric data. These data will be gathered and analyzed in order to evaluate the outcomes of the program. Biometric data includes a variety of proxy measures for autonomic nervous system function. The autonomic nervous system is composed of the parasympathetic and the sympathetic nervous systems and together they regulate cardiac, respiratory, and digestive functions. One gauge of autonomic nervous system function is heart rate variability (HRV) (Tiwari et al., 2021). HRV will be measured during sleep. HRV measures the intervals between heartbeats. Low HRV can reflect vagus nerve dysfunction (Lory et al., 2020). The vagus nerve helps to modulate nervous system responses, facilitating the activation and deactivation of the parasympathetic and sympathetic nervous systems. Previous research has linked low HRV with poor motor outcomes (Kalfiřt et al., 2023). Heart rate variability (HRV) along with resting heart rate will be measured during sleep using a commercial wearable device.

A second category of biometrics to be gathered is sleep data. Sleep is a key link in the chain of motor learning. New motor memories are consolidated during sleep (Astill et al., 2014). As such, several sleep measures will be utilized in this program, including total number of hours of sleep, total number of hours in bed, and respiratory rate during sleep. These metrics will also be gathered through the use of a wearable device.

Finally, urine analysis will be completed. Vanillylmandelic Acid (VMA) is a metabolite of norepinephrine and epinephrine excreted in the urine and serves as a proxy measure of these neurotransmitters. Norepinephrine and epinephrine are key neurotransmitters involved with motor learning. Homovanillic Acid (HMA) is a metabolite of dopamine and is also excreted in the urine and serves as a proxy measure. Dopamine is involved in the reinforcement and motivation element of motor learning.

In addition to biometric data, psychometric outcome measures will also be gathered. A standardized motor measure to assess fundamental motor skills is the Bruininks-Oseretsky Test of Motor Proficiency, 2nd edition (BOT-2). The BOT-2 is one of the most commonly utilized motor measures in the autism literature. Autism is poorly represented in the normative sample of most standardized motor tests (Wilson et al., 2018). However, the BOT-2 has established validity and reliability for this population (Downs et al., 2020). The BOT-2 is a widely used assessment tool designed to evaluate motor skills in individuals aged 4 to 21 years. It demonstrates strong reliability, with high internal consistency and test-retest reliability, ensuring consistent results over time. Additionally, the BOT-2 exhibits good validity, supported by its ability to accurately measure various components of motor proficiency, including fine motor precision, manual dexterity, balance, and coordination (Bruininks & Bruininks, 2005).

During phase two only, motor probes will be gathered. Probes are useful for assessing baseline behavior and monitoring progress in a single-subject design study. Motor probes were derived from existing standardized outcome measures that are commonly seen in autism research, including the Test of Gross Motor Development – Second Edition and the Movement Assessment Battery for Children – Second Edition, as well as common clinical observations (Henderson et al., 2007; Ulrich, A., 2000).

Phases two and three include goal attainment scaling (GAS). GAS will be utilized to provide a flexible and individualized measurement tool. Autism research is plagued by the heterogeneity of the autism population. GAS allows researchers to tailor goals specifically to each participant's level and provides a standardized method for quantifying progress, allowing for comparison across participants while accommodating varying baseline abilities. Additionally, the person-centered nature of GAS ensures that the outcomes reflect meaningful progress for each individual.

Because phase one is a case-control study investigating correlations between biological metrics and psychomotor metrics, there will only be one data collection time point. GAS and motor probes will not be implemented as part of this phase. Phase two is a single-subject design investigating the feasibility and cursory effectiveness of the adjunct intervention model (tVNS partnered with motor skill training). Data collection will include baseline data, followed by repeat measurements of motor probes, GAS progress, and sleep metrics after 6 hours, 12 hours, and 18 hours of intervention. Finally, the full battery of testing will be repeated at the termination of intervention after 24 hours of intervention. This same data collection pattern will be utilized for phase three, with the exception of motor probes which will not be utilized in this phase.

Important outcomes of this program include identifying which biological metrics correlate with psychomotor metrics (phase one); testing the feasibility of an adjunct intervention targeting biological factors along with motor factors (phase two); and examining the effectiveness of an adjunct intervention for increasing motor and functional outcomes (phase three).

Potential Barriers

This program targets motor skill deficits in autistic children involving a combination of biological adjunct interventions and occupational therapy. This is an innovative intervention that has not been utilized in this population for this purpose. Therefore, ethical considerations must be considered, particularly regarding the use of experimental interventions such as transcutaneous vagus nerve stimulation (tVNS) on vulnerable populations like children with autism. Informed consent will be obtained and this will outline potential drawbacks to participation in the studies. Families will be provided with plenty of time to read the informed consent and ask questions as they arise.

Participant recruitment and retention, especially within the specified age range (8–8 years 11 months old), may be challenging. It can be difficult to reach the threshold set by the power analysis; however financial incentives may be useful for addressing this problem. Incentives may help with barriers families face related to transportation or time commitments. This may also help with treatment adherence, as there can be a high cancelation rate in the pediatric population.

Obtaining necessary approvals from institutional review boards (IRBs) and regulatory agencies for conducting research involving human subjects, especially with novel interventions, can be challenging. The IRB at the host hospital will be engaged early in the process to try to ensure open communication to facilitate successful approval of the program.

Summary

This three-phase program attempts to expand upon our current knowledge of the biological mechanisms impacting motor skill acquisition in children with autism. From there, the feasibility of a novel intervention utilizing tVNS paired with motor skill training will be tested for feasibility using a single-subject design. Finally, a randomized controlled trial will be implemented based on knowledge acquired through phases one and two. This innovative intervention has the potential to improve outcomes in motor skill acquisition for children with autism. It also has the potential to highlight the unique and valuable contribution occupational therapy can contribute to the field of autism.

CHAPTER FIVE – Program Evaluation Research Plan

Although motor skill deficits in autistic children are pervasive, very little occupational therapy research has been conducted to evaluate effective intervention strategies. In the last decade, only 13 studies have been published investigating occupational therapy intervention for improving motor skills in autistic children (Ajzenman et al., 2013; Alaniz et al., 2017; Alkhalifah et al., 2022; Collins et al., 2015; Hilton et al., 2014; Hirschmann et al., 2023; Iwanga et al., 2014; Jin et al., 2023; Kumar & Nagalakshmi, 2023; Lopez & Kume, 2018; Nuntanee & Daranee, 2019; Schoen et al., 2020; Walsh et al., 2021). Furthermore, intervention research in the larger context of autism therapy reveals a lack of theory base driving the interventions studied. This is, in part, due to the poor understanding of the divergent autism brain and its interplay with the development of motor skills. This three-phase research study will begin to develop the path forward to more evidence-based interventions for occupational therapy practitioners (OTPs).

The study will be delivered on-site in a Southern California outpatient pediatric clinic. The author is the primary investigator and will lead a team of practitioners in implementing the program. There are several intended users of the research findings. First and foremost, autistic children and their families will benefit from the knowledge gained through this investigation. The disseminated information will also help the larger population of OTPs working in partnership with autistic clients. Finally, results will be useful for advocacy to further fund and develop similar programs, as well as improving occupational therapy's stature in the general public's awareness.

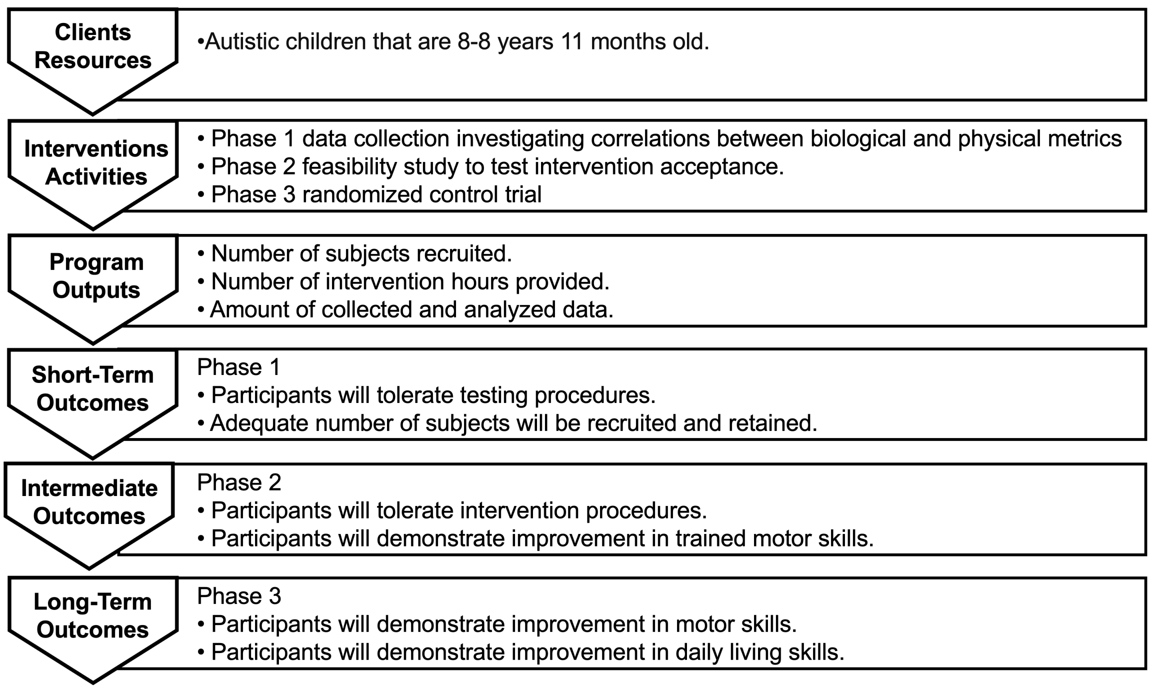
Vision

The vision of this program is to develop a precision intervention for autism treatment. Precision medicine is when treatment is tailored to an individual's phenotype, environment, and lifestyle. A phenotype, "simply refers to an observable trait" (NIH, 2023). Phenotypes provide a personal profile that allows interventions to be customized to the person. Precision medicine is an emerging field of study and has made gains in fields such as oncology but autism treatment lags behind significantly. Researchers are investigating genetic patterns for autism, but the field is still relatively new and ineffective for identifying widespread, clinically meaningful autism phenotypes (Kalin, 2021; Matta et al., 2022; Nisar et al., 2019). Studies have also described anatomical differences as well as neurotransmitter deficiencies in the autistic brain (Marotta et al., 2020). However, this type of diagnostic testing can be difficult to tolerate or contraindicated for use in healthy children, so it is not part of routine clinical care (American Academy of Pediatrics, 2020). Therefore, the next clinical step in developing precision intervention for children with autism is to identify biomarkers via non-invasive means. From there, researchers can link biometrics to psychometrics which may allow for more effective interventions targeting both biological factors and functional outcomes.

This program also helps to address disparities in healthcare access by driving functional gains with less dosing. This is a critical need in the United States where healthcare coverage is not a guaranteed right, and benefits vary widely based on socioeconomics. Finally, this program advances scientific knowledge by conducting research that aims to deepen our understanding of the mechanism of autism and an individual's response to intervention. Figure 5.1 illustrates the steps to achieving this vision.

Figure 5.1

Simplified Logic Model



Program Evaluation Research Questions

Formative and summative research questions play important roles in the research process. Formative questions are crucial for shaping the early stages of a study, helping to define the scope, purpose, and methodology. Additionally, formative questions allow for iterative feedback, enabling adjustments based on emerging insights. Summative questions serve as the final evaluation metrics, providing a comprehensive assessment of the study's outcomes. Quantitative data collection procedures are listed in the methods section. Qualitative data collection will occur via post-intervention interviews with the treating practitioners and participant families at the completion of phase two. Table 5.1 summarizes formative and summative questions as they relate to each stakeholder.

Table 5.1

Stakeholder Program Evaluation and Research Questions

Stakeholder	Research Questions
Primary Investigator	Formative: Did biometrics correlate with physical metrics? Was the intervention tolerated by the clients? Was the intervention provided with fidelity? Can funding be secured for the project? Summative: To what extent did biometrics correlate with psychometrics? To what extent did the intervention improve motor skills? To what extend did the intervention improve daily living skills? Can the data be used to advocate for increased funding for OT services?
Program Staff	Formative: Was the intervention feasible to implement? Was the manual easy to follow and understand? Were some of the aspects of the program easier to implement than others? Is there anything that should be changed to improve the program manual or intervention delivery? Summative: Was fidelity established with intervention implementation?
Program Participants/ Families	Formative: Were the test procedures tolerable? Was the intervention tolerable? Summative: Did the intervention improve identified skills?

Director of Research	Formative: Does the study contribute to knowledge that would benefit the hospital's clients? Does the intervention comply with licensing and compliance? Is the intervention safe for clients? Summative: Will the research data show a clinically meaningful improvement on the dependent variable? Can the research data contribute to improved quality of care for existing and future clients? What was the attrition rate of participants? Can the study be published in a peer-reviewed journal?

Methods

Participants

Children between the ages of 8 years and 8 years 11 months old are the targeted population for this program. Phase one will include both neurotypical and autistic children whereas phases two and three will include only autistic children. A power analysis will be completed to determine the necessary sample sizes. Subjects will be recruited using flyers, emails, and social media as well as drawing from the clinical population currently receiving treatment at Casa Colina Hospital and Centers for Healthcare in Pomona, California. Subjects will be financially incentivized by receiving compensation for their participation. All testing and intervention will be completed at the Children's Services Center on the Casa Colina Pomona campus.

Subjects will be screened for autism utilizing the Gilliam Autism Rating Scale, third edition (GARS-3) (Gilliam, 2013). Motor skills will be analyzed using the Bruininks-Oseretsky Test of Motor Proficiency, 2nd edition, full battery (BOT-2)

(Bruininks & Bruininks, 2005). Inclusion criteria for the autism group will include; primary diagnosis of autism, confirmed by the GARS-3; motor delay as evidenced by at least one standard deviation below the norm on at least one subtest of the BOT-2 (phases two and three); and ability to complete the study elements. Exclusion criteria for the autism group include presence of cardiac, respiratory, psychiatric, or seizure disorders; disorders of autonomic dysfunction; Down syndrome, Fragile-X or other genetic-based disorders; presence of psychiatric medication use; and/or presence of acute infections. Inclusion criteria for the neurotypical group will include: ability to complete the study elements. Exclusion criteria for the neurotypical group include presence of autism as indicated by the GARS-3; presence of autistic siblings; presence of cardiac, respiratory, psychiatric, or seizure disorders; disorder of autonomic dysfunction; Down syndrome, Fragile-X or other genetic-based disorders; presence of psychiatric medication use; and/or presence of acute infections.

Procedures

The Institutional Review Board (IRB) at Casa Colina's Research Institute will provide oversite to these studies. Informed consent forms will be approved by the IRB and reviewed with the patient and the family prior to enrollment in the study. Subject number assignment linked to protected health information (PHI) will be stored separately from the scoring data. Data sheets will be turned into the primary investigator and entered into the tracking log on a password protected computer. Data sheets will be stored in a fireproof chart storage unit.

This is a three-phase study consisting of a case-control correlative study (phase one), single subject feasibility design (phase two) and a randomized controlled trial (phase three).

Measures

Biometric Attributes. Biometric data will be gathered via a wearable device and urine samples. Wearable device information will be downloaded during the targeted intervention sessions. Urine samples will be sent to an outside lab for analysis. Biometrics will include:

- Heart rate variability (HRV) during sleep
- Resting heart rate average during sleep
- Total number of hours of sleep
- Total number of hours in bed
- Respiratory rate during sleep
- Vanillylmandelic Acid (VMA)
- Homovanillic Acid (HVA)

These measures assist in investigating the autonomic nervous system function of individuals with autism, utilizing non-invasive techniques. VMA and HVA are metabolites of catecholamines (Gątarek & Kałużna-Czaplińska, 2022). They are analyzed by urine samples and provide a non-invasive measure of the autonomic nervous system and vagus nerve function (Bharath et al., 2019). The utilization of HRV and sleep tracking provide proxies for autonomic function (Tiwari et al., 2021; Walker et al., 2005).

Psychomotor Attributes. Testing will be completed by evaluators who are licensed and registered occupational practitioners. They will be blinded to group allocation and temporal aspects of the study. Psychometrics will include:

Gilliam Autism Rating Scale, Third Edition (GARS-3). The GARS-3 is an autism assessment utilized in all three phases of this program to confirm the diagnosis of autism. The GARS-3 is a standardized measure with high sensitivity and specificity and it is commonly represented in the autism literature (Gilliam, 2014).

***Goal Attainment Scaling*.** Goal attainment scaling (GAS) is a personalized, client-driven outcome measure that can create standardized results by utilizing a clear framework for setting goals and measuring goal attainment. Goals are derived in collaboration with the family/ client and are formulated to demonstrate five levels of outcomes. The levels are written in a manner that provides an equal distance of change between each level. This allows the scores to be translated into T scores for statistical analysis. GAS is commonly used in the autistic population due to high heterogeneity in the study population as well as a lack of sensitivity in existing standardized measures (Lee et al., 2022; Wilson et al., 2018). In this study, GAS will be utilized for phases two and three. First, an independent evaluator will conduct a semi-structured interview with the family and client at baseline testing to determine three motor skills that are salient for measurement. Performance towards GAS goals will be videotaped and the goals will be scaled on a five-point scale with -2 representing baseline, -1 representing somewhat worse achievement than expected, 0 representing expected achievement, +1 representing somewhat better achievement than expected, and +2 representing much better achievement than expected. In phase two of the study, GAS goal testing will be administered at the beginning of the first intervention session and the end of each subsequent session. This will allow for sufficient data points for analysis in the single-subject design. In phase three of the study, GAS goal testing will be administered at the first intervention session and re-administered after session six, 12, 18, and 24. GAS testing will be video recorded. The videos will be rated by an evaluating practitioner via video review. Videos will be presented randomly to ensure that the rating practitioner will be blinded to group allocation and temporal aspects of the study.

Probes. Three motor probes have been identified for use in phase two of this study. Probes are useful for assessing baseline behavior and monitoring progress in a single-subject study. Motor probes were derived from existing standardized outcome measures that are commonly seen in autism research, including the Test of Gross Motor Development – Second Edition and the Movement Assessment Battery for Children-Second Edition, as well as common clinical observations (Henderson et al., 2007; Ulrich, A., 2000). Each probe will be administered two times per week by the evaluating therapist until a stable baseline emerges. The intervention will begin once a baseline is established. During the intervention stage, the probes will be administered twice a week by the treating therapist.

The first motor probe will be a timed up-and-go test. The participant will start seated in a chair that is fitted for the participant (creating an ergonomically correct, 90-degree bend in the knee with both feet flat on the floor). The participant will stand up, walk 10 feet, turn around, walk back, and sit down again. Participants will be allowed two trials with coaching before measurement begins. Participants will be instructed to move as fast as they safely can. Proper execution involves crossing the ten-foot mark and then returning to a seated position. The timer will begin with the command “go” and end when the participant’s bottom touches the chair’s seat. The task will be executed twice with the fastest time of the two trials recorded. Time will be recorded to the 100^{th} of the second.

The second probe will be a block-stacking task. The participants will stack as many one-inch wooden blocks as they can without having them tip over. The participant will be given two trials with coaching before measurement begins. Participants will be instructed to stack as many blocks as they can without having the tower fall. The last block placed that causes the tower to fall will not be counted. The task will be executed twice with the highest number of blocks stacked recorded.

The final probe will be the stair climb test. The participant will climb 14 steps (eight-inch step height). No trials will be provided. Participants will be instructed to go up and down the flight of stairs as quickly as they safely can. Encouragement and directives will be provided during the test to ensure the participant ascends and descends the entire flight of stairs. The timer will begin with the command “go” and end when both feet of the participant strike the ground after descending the final stair. Time will be recorded to the 100^{th} of the second.

Bruininks-Oseretsky Test of Motor Proficiency – Second Edition, full battery. The Bruininks-Oseretsky Test of Motor Proficiency – Second Edition (BOT-2) is a standardized assessment that is commonly utilized in the autism literature to characterize motor skills (Battah et al., 2023). The assessment measures fine motor and gross motor abilities in people ages four to 21 years old and is one of the few motor skills tests that included autistic people in the normative population sample. The test consists of eight subtests with 53 items grouped into fine manual control, manual coordination, body coordination, and strength and agility. The test demonstrates high test-retest reliability with subtests ranging from 0.70 to 0.90 or higher and has strong content and construct validity (Bruininks & Bruininks, 2005).

Vineland Adaptive Behavior Scales, Third Edition (Vineland-3). The Vineland-3 is a proxy measure of adaptive behavior that is commonly represented in the autism research (Chatham et al., 2018). The parent or caregiver form will be utilized in all three phases of this program. It will be used to measure functioning in five domains: communication, daily living skills, socialization, motor skills and maladaptive behavior index. The Vineland-3 has been validated with the autism population and has high test-retest reliability with subtests ranging from 0.91 to 0.94, with excellent internal consistency and concurrent validity (Sparrow et al., 2005).

Interventions

Phase One

This phase will be a case-control, correlative study design. Children who meet the inclusion criteria will be assigned to a neurotypical control group or an age and sex-matched autistic group. The GARS-3, BOT-2, and Vineland-3 will be provided by trained and licensed occupational therapy practitioners following standardized procedures that are described in the outcome measures' manuals. Parents will receive face-to-face instruction on the use of the wearable device and procedures for gathering biometric data. They will also receive a written protocol for their reference. Parents will receive daily notification reminders to upload biometric data to provided mobile devices. Sleep metrics will be gathered daily for a two-week period. Urine collection will occur once during the testing session at the clinic. Laboratory biometric data will be processed at a third-party location that has established proficiency and accuracy in administering identified tests.

Phase Two

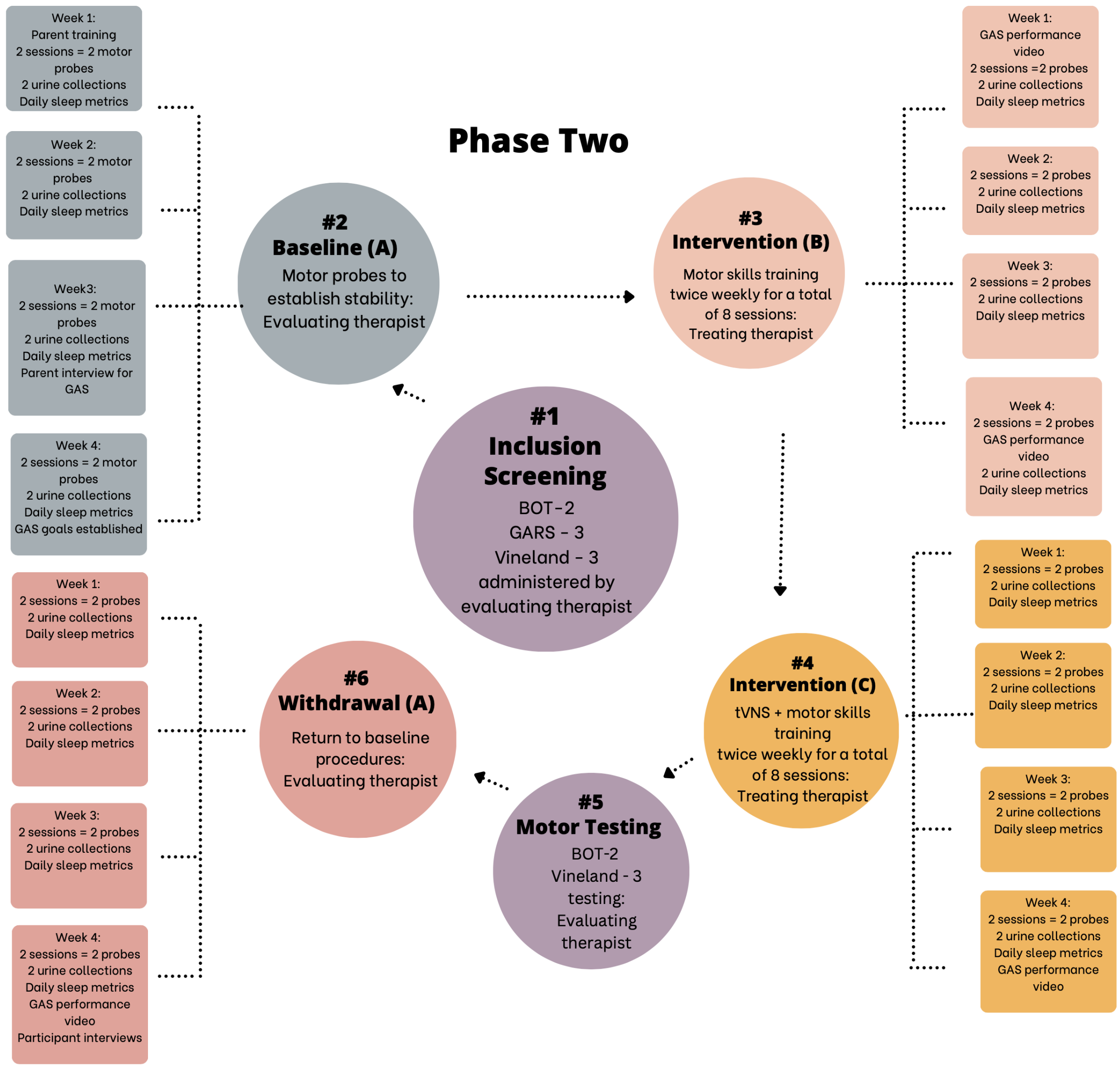
This phase will be an A-B-C-A single-subject design. GARS-3 and BOT-2 testing will be completed prior to the first baseline visit to establish inclusion criteria are met. At the first baseline visit, parents will receive the above-detailed training on the use of the wearable device and data collection procedures. Bi-weekly urine collection and daily sleep data will occur during baseline and throughout the duration of the study. During baseline, the Vineland-3 will be administered and parents will be interviewed for goal attainment scaling. Three goals will be identified and scaled. In addition, bi-weekly measurements of the motor probes will be collected until stability is established. Based on previous work done by Andelin et al. (2021), baseline stability will be defined as three consecutive data points with less than 20% variance.

After a stable motor baseline is established (A), motor skill training will be implemented (B), followed by motor skill training paired with tVNS application (C), with a return to baseline procedures (A). Each stage will last for four weeks for a total of eight sessions per stage. The total duration of phase one will be approximately 16 weeks (depending on the length of baseline) and consist of 24 intervention sessions (two sessions per week).

During the intervention period, participants will be seen twice a week for 50-minute sessions. Sessions will include motor skill training (B) for four weeks with a total of eight sessions. The intervention will follow a manualized procedure starting with 20 minutes of table play followed by 30 minutes of motor skill training (10 minutes targeting each of the goal areas). The second intervention block (C) will be four weeks with a total of eight sessions and will include tVNS stimulation for 20 minutes following parameters established by previous research (Jin & Kong, 2016; Li et al., 2022). The stimulation parameters will be set at 0.3-ms square pulses at 20 Hz for 30 seconds repeated every 5 minutes for a total of 20 minutes. During this time, participants will be seated at a table with preferred toys/ activities/ media to keep them occupied. The stimulation period will immediately be followed by 30 minutes of motor skill training following a manualized procedure (10 minutes targeting each of the goal areas). Psychomotor testing will be implemented following stage C and prior to the withdrawal stage. Qualitative data will be gathered during the withdrawal block via semi-structured interviews with the families, participants, and interventionists. Figure 5.2 demonstrates these activities.

Figure 5.2

Phase Two Activity Timeline



Note: Bruininks-Oseretsky Test of Motor Proficiency, second edition (BOT-2); Gilliam Autism Rating Scale, third edition (GARS-3); Vineland Adaptive Behavior Scales, third edition (Vineland-3); transcutaneous vagus nerve stimulation (tVNS)

Phase Three

This phase is a randomized controlled trial in which the pre- and post-intervention scores will be compared between two matched groups of autistic children: an intervention using tVNS adjunct motor skill training compared to a treatment-as-usual control group. Treatment-as-usual is defined by the participants' current school and therapy regimen. Data from both groups related to these services will be collected and analyzed. Baseline testing will consist of the GARS-3, BOT-2, and Vineland-3 testing and goals will be set for GAS using above stated procedures. Children will be randomly assigned to the intervention or control group using sing GraphPad Prism version 10.0.0 for Windows, GraphPad Software, Boston, Massachusetts USA, www.graphpad.com. Biometric data collection will be initiated at baseline testing following the above-stated parent training procedure. Urine will be collected at pre- and post-testing sessions. Sleep data will be measured and uploaded daily starting at baseline testing and ending at post-intervention testing. The intervention will be provided bi-weekly for a total of 24, 50-minute sessions following the above-detailed procedure for tVNS adjunct motor skill training.

Fidelity

Fidelity checks will be utilized to ensure intervention follows the manualized procedures. Intervention sessions will be videotaped and 10% will be randomly chosen for video review by the primary investigator to ensure fidelity.

Threats to Internal Validity

Preserving internal validity is crucial in to all three phases of this study. To mitigate the threat of history, meticulous control and standardization of the clinical environment will be upheld, ensuring repeatability. In pediatric studies, maturation poses a consistent challenge. Scheduling sessions twice a week serves to compress the study duration, reducing the impact of this threat. To counter the risk of repeat testing, Goal Attainment Scaling was deliberately chosen and will be reviewed for scoring in a random order. Consistency in instrumentation will be maintained by adhering strictly to established laboratory protocols for urine collection and analysis. Finally, video reviews will be utilized to monitor and prevent any potential diffusion of treatment.

Data Analysis

Quantitative data will be analyzed using JMP (JMP Statistical Discovery from SAS, Carey, NC). Qualitative data will be organized and coded and analyzed by NVivo Software (NVivo version 14, QSR International Pty Ltd, www.lumivero.com). Phase one quantitative data will be analyzed using correlative statistics. Phase two qualitative data will be analyzed first by using visual analysis. Findings will be graphed and analyzed for changes in level, latency of change, trend and slope. Visual inspection will be confirmed by using C and Z statistics. Phase two and three quantitative data will be analyzed using samples t-test for normally distributed data. For nonparametric data, Mann-Whitney U will be utilized. GAS data will be assessed using Wilcoxon signed rank to compare pre and post-intervention.

Conclusion

This three-phase program aims to start addressing the complex issue of motor skill delays that are common among individuals with autism. The first phase aims to establish motor phenotypes by analyzing patterns in the correlations between biometric and psychometric data. The second phase assesses the feasibility of implementing a novel intervention that targets both biological and physical factors. Finally, the third phase seeks to establish the effectiveness of the intervention on a larger scale population.

CHAPTER SIX – Dissemination Plan

Introduction

Autism is a complex neurodevelopmental disorder that impacts how a person communicates, behaves, and socially interacts (American Psychiatric Association, 2013). Many people with autism have motor coordination impairments (Bhat, 2020). This affects their ability to participate in activities they want and need to do (Ozboke et al., 2021). One explanation for these differences is found in the structural and functional differences of the autistic brain. Current occupational therapy practice rarely accounts for these differences. This three-phase study starts with investigating connections between motor skill presentation and biological measurements. From there, a motor phenotype can be developed to help guide interventions. The second phase of this program is a feasibility study to determine if an adjunct intervention utilizing vagal nerve stimulation during motor training will be tolerated by autistic children. Finally, the third phase explores the effectiveness of this intervention approach.

Dissemination Goals

The long-term goal of this program is to innovate, implement, and promote interventions that have a meaningful impact on the lives of children with autism. This goal is achieved through increasing scientific understanding in the field of autism. The primary short-term goal of this program is the timely publication of each phase of the study. Sharing research results is important to building knowledge in the field of autism. By engaging in knowledge dissemination, researchers can build on the work of others. This type of knowledge construction exponentially increases understanding and furthers the scientific process. In addition, publishing research findings in a peer-reviewed journal increases accountability resulting in a higher quality of work. The scrutiny of peers is the best way to identify potential flaws or limitations in a study Also, each publication contributes to the validity of the next phase, which can increase funding opportunities for the program. In addition to publication, rapid dissemination can occur through social media and conference presentations. Social media allows for a wider reach to a more diverse audience. Similarly, conference presentations are often more accessible and consumable to clinicians outside the academic circle, particularly when compared with the challenges of sourcing, obtaining, and analyzing a research study.

Target Audiences

The primary audience of this program is the professionals who work with autistic children, particularly occupational therapy practitioners. This research can inform their practice and enable them to provide more effective interventions. Parents of children with autism are also important stakeholders making them a salient secondary audience of this program.

Key Message – Interventionists

An innovative research program is now underway to develop precision intervention methods tailored to the distinct presentation of each individual with autism. Rather than taking a one-size-fits-all approach, this research recognizes that autism manifests differently in every person and aims to increase our understanding of these distinct characteristics. The vision is to identify a motor phenotype for each child, using patterns in biometrics and psychometric measurements, that will help guide intervention choices. From there, an intervention can be provided that will directly impact neuromodulation, increasing neuroplasticity while motor skill interventions are being implemented. This may result in increased motor skill gains in a shorter amount of time. Stay up to date on the studies as they are published and considering trying the methods in the clinical setting. Together, we can move away from generalized autism interventions toward a future of truly individualized, precision support designed for each unique client on the spectrum.

Key Message – Caregivers of Children with Autism

Caregivers of autistic children may have noticed differences in their child’s motor skills compared to neurotypical peers. These differences can manifest in various ways, such as challenges with coordination, daily living skills, or fine motor tasks. This research aims to shed light on the underlying mechanisms behind these differences. By exploring the biological underpinnings of motor skill development in autism, researchers hope to gain insights that can lead to more personalized and effective interventions. At the same time, it is important to recognize that differences in motor skills are a part of the neurodiversity spectrum. This research does not aim to "cure" or "fix" these differences but rather to understand them better. The goal is to provide families with the tools and support they need.

Information Advocates

Autistic voices and perspectives are essential to the meaningful dissemination of these findings. As a marginalized group that has historically been excluded from research about them, collaborating with a credible, autistic spokesperson is essential.

Temple Grandin is one of the most influential autistic spokespersons in the world. Her published books were among the first to publicly share insights about the autistic experience. She went on to have a successful career revolutionizing the practices for the humane handling of livestock. She has been inducted into the National Women's Hall of Fame and has been named one of Time's 100 Most Influential People (Hauser, 2010). Her life was featured in a film that won several Emmy and Golden Globe awards (Vozick-Levinson, 2020). Her success as a speaker, author, and consultant has served as a megaphone to send her message to the masses. Temple Grandin often discusses her experiences as an autistic person. She has discussed her motor delays and difficulty with motor coordination (Attwood, n.d.). In addition, she has served as a strong advocate for intervention for autistic children (Keltner, 2023). As such, she would be a meaningful and credible spokesperson for this program. In addition, Temple Grandin has presented at Casa Colina's Autism Conference in the past making her a potential reachable spokesperson.

Claudia Hilton is an associate professor and occupational therapist at the University of Texas Medical Branch. She has established herself as a credible and pioneering researcher in the area of motor skill impairments in children with autism and would be an effective spokesperson for communicating findings to the occupational therapy community. Hilton's groundbreaking 2012 study was the first to comprehensively evaluate motor deficits in children with autism compared to their non-autistic siblings (Hilton et al., 2012). Her research found that 83% of autistic children had below-average motor skills, highlighting these impairments as a core characteristic linked to the autism diagnosis itself. This background allows her to speak authoritatively on translating motor skill interventions into effective clinical practice making her a highly credible spokesperson to communicate findings from this program.

Dissemination Activities

Communicating the results of the research findings is crucial to the goals and objectives of this program. A multi-pronged approach leveraging various communication channels will be employed to share the findings with the key audiences identified in this chapter as well as the public at large. The primary investigator has extensive experience with all of the planned activities described below and will be the responsible party for implementing these activities. Table 6.1 summarizes the budget for these activities.

Electronic Media

Electronic media will be the first approach to disseminating findings since it is the quickest and most direct way of sharing information. The electronic media approach will be twofold. First, the extant literature as it relates to autism and motor skills intervention will be shared in bite-sized videos on YouTube. Social media platforms like YouTube allow the investigator to engage with an extensive and diverse audience, including the primary and secondary audiences identified earlier in this chapter. These videos can be produced and published while the funding for the program is being secured. Not only is this an effective method for gaining an interested audience but it also can be utilized to build credibility with granting agencies. As findings are established, continued output of videos will be published on the YouTube channel.

Person-to-Person Contact

The next dissemination activity will be conference presentations. Conferences offer the opportunity to share the research with a large audience of professionals. The first targeted conference will be the American Occupational Therapy Association (AOTA) Annual Conference (AOTA, n.d.). This allows increased visibility with the primary audience. Conference presentations also facilitate constructive feedback and critical discussions with other professionals that can refine and strengthen future phases of the research.

The second conference targeted will be the International Society for Autism Research (INSAR) conference. This organization exists to advance research in the field of autism (INSAR, n.d.). Disseminating findings at this conference has many benefits to the program. First, the knowledgeable audience can spark new ideas, collaborations, and potential avenues for future research. In addition, autism-focused conferences provide a unique networking environment where the work can be highlighted and the primary investigator can be positioned as a trusted source of information on the topic. This may open doors to new funding opportunities for the program.

Written Information

The final effort for dissemination will be the publication of results in peer-reviewed journals. Each phase will be submitted for publication in journals such as the American Journal of Occupational Therapy (AJOT) and the Journal of Autism and Developmental Disorders (JADD). These reputable journals will allow the work to be discovered by the primary and secondary audiences. Findings will emphasize the dimensions of merit, worth, significance, and probity. Caution will be taken not to overinterpret or misinterpret results. Discussion of suggestions for clinicians to consider in treatment, suggestions for future research, and identification of study limitations will be described. Finally, a plain language summary will be provided to ensure the findings are consumable for people with autism and their families as well as clinicians unfamiliar with the topic.

Table 6.1

Budget for Dissemination Plan

Electronic Media		
Activity	Hours Required	Amount
Video script writing and recording (15 videos)	30	$2,760
Video design and editing	30	$2,760
Total:		$5,520
Person-to-Person Contact		
Activity	Hours Required	Amount
AOTA attendance and travel (3 years)	--	$7,800
INSAR attendance and travel (3 years)	--	$9,600
Total:		$17,400
Written Information		
Activity	Hours Required	Amount
Report writing (3 reports)	240	$22,080
Report revisions and editing (3 reports)	240	$22,080
Total:		$44,160
Total Dissemination Plan:		$67,080

Evaluation

To evaluate the results of the dissemination efforts, measurable criteria for each activity have been identified. These outcomes demonstrate the impact and reach of the chosen approaches. Electronic media efforts will be measured using website analytics. YouTube offers analytics through its platform describing detailed insights regarding the performance of posted videos. Metrics include data such as the total views, viewer engagement, number of subscribers, and audience retention. Person-to-person contact efforts will be measured on attendance and engagement metrics. Written information efforts will be evaluated on publication success and citations. Table 6.2 describes the metrics set for the program.

Table 6.2

Evaluation Outcomes

Electronic Media		
Metric	Description	Criteria
Total views per video	The total number of times the video has been watch gauges the reach of the video.	In the first month, video will be viewed a minimum of 100 times.
Viewer engagement	The total number of likes, comments or shares a video receives.	Each video will reach an engagement rate of 5% of the total views.
Number of subscribers	The total number of viewers who have subscribed to the channel.	The channel will gain 10 subscribers in the first month.
Audience retention	The percentage of a video watched over time.	The average watch time of the video will be 40% of the total length.
Person-to-Person Contact		
Metric	Description	Criteria
Attendance	Number of audience members at each presentation	50 participants
Engagement	Rating on Course Survey	90% or higher
Written Information		
Metric	Description	Criteria
Publications	Number of accepted publications in a peer-reviewed journal	2 publications
Citation Rate	Closed access citation per publication average	16 citations per publication

Conclusion

The comprehensive dissemination strategy outlined in this chapter will ensure that the findings of the studies reach and resonate with the target audience. By using electronic media, person-to-person contact, and written information, the findings will reach autistic individuals and the clinicians who work with them. Also, utilizing a broad communication approach ensures that the information will be accessible to a diverse audience. The dissemination activities are evaluated using specific and measurable outcomes, which will allow systematic evaluation of the effectiveness of the planned activities. By tracking these metrics, valuable information will be gained allowing for data-driven decision-making on future phases of the program.

CHAPTER SEVEN – Funding Plan

Mark Twain wisely said, "The lack of money is the root of all evil" (as cited in Tuckey, 1980). When it comes to research, this is certainly a true statement. A funding plan is essential to ensure a program has the money required to launch and maintain sustainability. This chapter outlines the local resources, budget allocation, and potential funding sources for a three-phase research program.

This program is a three-phase study investigating the connection between biometrics and psychometrics in children with autism to develop more targeted interventions for improving motor skills. Phase one consists of a case-control research design that assesses correlations between biometrics and psychometrics in children with autism as compared to neurotypical peers. This will allow for identifying a basic motor skill phenotype for autism. This phenotype may identify what type of children will most benefit from the intervention deployed in subsequent phases. Phase two is a single-subject design establishing the feasibility of using tVNS as a neuromodulator to support motor skill training. Finally, phase three consists of a randomized control trial to evaluate the effectiveness of the intervention.

Local Resources

This research program will be implemented at Casa Colina Hospital and Centers for Healthcare in Pomona, California. Casa Colina has a long history of service in Southern California. The hospital has a well-established volunteer program that is continually supported by members of the community as well as local college students. Phase one will require the help of this small volunteer army to support subject recruitment. Recruitment can be the source of pain in any research study and phase one will likely require high recruitment numbers to establish statistically significant correlations. The hospital’s volunteers will assist in developing, printing, and distributing flyers throughout the community to help with recruitment.

Phase two of the program will require extensive data collection owning to its single subject design. In addition, treatment fidelity will be measured via video review. This can be a laborious task. Casa Colina will tap into its university relationships to assist with this aspect of the study and recruit level two occupational therapy fieldwork students to help facilitate this activity.

Budget Allocation

Research is a capital-intensive endeavor. Table 7.1 overviews the full budget for each phase of this program. For additional details on the budget line items, see Appendix B. Personnel are the largest expenditure in the budget. Personnel expenses include each evaluator and interventionist's fully loaded, hourly rate (including salary and benefits) and the salary fees for the primary investigator and research support staff. Research support staff include the director of research who will oversee the program as well as the statistician who will support data analysis. Trained volunteers and students will support data collection efforts at no added expense. In addition, the host hospital (Casa Colina) will provide in-kind donations to cover expenses related to scheduling, admissions procedures, photocopying, and other office supply expenses. The host hospital will also donate the clinical space at no expense to the program. Finally, the host hospital will support grant-writing activities.

Table 7.1

Budget Overview for Phase One-Three

Phase One		
Category	Donor Amount	In Kind Donation
Personnel	$22,778	$11,662
Outcomes and Participants	$15,974	$5,098
Dissemination	$4,120	$3,520
Total	$42,873	$20,280
Toal Amount for Phase One: $63,153		

Phase Two		
Category	Donor Amount	In Kind Donation
Personnel	$19,912	$23,592
Outcomes and Participants	$1,070	$4,823
Clinical Supplies	$3,260	$360
Dissemination	$4,120	$3,520
Total	$28,362	$32,295
Toal Amount for Phase Two: $60,657		

Phase Three		
Category	Donor Amount	In Kind Donation
Personnel	$59,116	$25,720
Outcomes and Participants	$7,776	$17,920
Clinical Supplies	$12,388	$3620
Dissemination	$4,120	$3,520
Total	$83,400	$50,780
Toal Amount for Phase Three: $134,180		

Pediatric therapy requires a significant amount of clinical supplies and equipment to be successful. The host hospital will provide all necessary clinical equipment (such as swings, climbing equipment, toys, tables, craft supplies, etc.) at no expense to the program. Grant funding will support the attainment of standardized tests and protocol booklets. Grant funding will also support the purchase of the tVNS units, wearable devices, video recording device, and laboratory fees. Finally, participants will be compensated for their participation in the study. This element is essential for recruitment and retaining subjects. Grant funding will also support this item of the budget.

Potential Funding Sources

In-Kind Donations

First and foremost, the host hospital will provide significant funding for this program. Casa Colina Hospital and Centers for Rehabilitation has a deep commitment to contributing to innovative rehabilitation research studies. The hospital has a Research Institute, funded by the Casa Colina Foundation, which supports all studies on campus with in-kind donations. For example, the Foundation fully funded a pediatric research project investigating the impact of aquatic occupational therapy on drowning prevention skills in autistic children (Alaniz et al., 2017). The backing of the Director of Research is imperative to secure these resources. Support has already been gained for phase one of this program and grant applications have been initiated. Ongoing meetings between the primary investigator and the Director of Research will continue throughout the implementation of this multi-phase program to ensure continued support.

Potential Granting Agencies

Grant funding is imperative for this program to move forward. As a 501(c)3 organization, Casa Colina has a grant writer on staff and an extensive network of relationships with granting agencies, including the National Institute of Health (NIH). An initial grant submission to fund phase one of the program has been submitted to the Autism Science Foundation (ASF). ASF emphasizes the support of cutting-edge research that has the potential to positively impact people with autism (ASF, 2024). An example of a recent project funded by ASF is the Autism Baby Siblings Research Consortium (BSRC). The BSRC is actively working to identify behavioral and biological metrics for autism (Baby Siblings Research Consortium, n.d.). This is similar to the aim of phase one of this project which seeks to establish a motor skills phenotype based on biological metrics correlated with physical metrics. As such, the ASF is a good match for phase one funding.

Securing grant funding requires a high-volume approach to be successful. Therefore, many additional potential granting agencies have been identified. Funding sources that emphasize work with autistic children have been prioritized. For phase one, granting agencies that focus on developing evidence on the science of autism will be targeted. In addition to ASF, another example of this type of granting agency is the Simons Foundation. The Simons Foundation offers pilot awards to provide initial support to seed new ideas in the field of autism (Simons Foundation, n.d.). An example of a recently funded project through the Simons Foundation is an investigation of neural networks that link to aggression in autism. Researchers are attempting to identify a neurological phenotype that can enable the creation of more targeted neuromodulation interventions for reducing aggression (Simons Foundation, 2024). As illustrated by this project, the Simons Foundation is another good match for potential funding of phase one.

For phases two and three of the program, granting agencies that prioritize innovative interventions will be solicited. One successful relationship that the host hospital has a long-standing relationship with is the San Manuel Band of Mission Indians. Currently, the hospital is managing a $450,000 grant donated by the Tribe to support the development of an innovative use of music to support therapeutic gains. Phase two is particularly suited to this type of business foundation because of its emphasis on clinically meaningful outcomes and collaboration with participating families.

Alternative granting agencies at this level include organizations like Autism Speaks. Autism Speaks contributes to research in the field of autism that may improve the lives of autistic people today as well as generate solutions for the future (Autism Speaks, n.d.). This is a natural fit for the current research proposal. If the innovation in phase two is proven effective, it could improve functional outcomes for people with autism. It also has the potential to disrupt early motor skill delays which may have a cascading impact on development. Finally, this innovation could potentially reduce dosing making intervention more accessible. An example of a comparable grant that Autism Speaks has funded is a Vanderbilt pilot study. This study examined the impact of melatonin on sleep in children with autism. Autism Speaks contributed $100,000 to support this effort (Autism Speaks, n.d.-a).

As a randomized controlled trial, phase three will be the most expensive phase of the program. The multi-phase approach of this program was designed, in part, to help ensure that this level of funding will be obtainable. By establishing preliminary data via phases one and two, large granting agencies such as the NIH will be more likely to consider the study as a candidate. In addition, it may be beneficial at this level to partner with one of Casa Colina's University collaborators, such as the University of Southern California (USC) or the University of California, Los Angeles (UCLA). These partnerships make applicants more appealing to the NIH.

Additional organizations that may fund at this level include the Organization for Autism Research (OAR). OAR focuses on applied research to support the daily living of people with autism (OAR, 2022a). This clearly aligns with the goals of phase three. An example of a recently funded project by OAR includes a study investigating the key ingredients in physical activity interventions for supporting motor competence in autistic people (OAR, 2022). Table 7.2 summarizes these potential funding sources and the expected contribution each can make towards the project.

Table 7.2

Potential Funding Sources Contribution

Granting Agency	Expected Amount of Contribution
Autism Science Foundation	$45,000
The Simons Foundation	$45,000
San Manuel Band of Mission Indians	$30,000
Autism Speaks	$85,000

Private Donors

Finally, private donors will also be a potential funding source for a portion of this program. Casa Colina has wide-ranging relationships with private donors in the community. These donors may be solicited to help support the research effort. Solicitation may occur via mailings, personal conversations, or large-scale fundraising efforts (such as a Gala).

Conclusion

Funding a research program is a challenging endeavor that requires strategic planning. Leveraging community volunteers, occupational therapy students, and in-kind donations from the host hospital can offset significant costs. Granting agencies offer another crucial source of funding. Targeting applications to agencies with aligned priorities can secure substantial financial support. Additionally, private donations can significantly bolster the program's finances. Overall, the diversity of funding sources creates a robust foundation for this research program.

CHAPTER EIGHT – Conclusion

Autism is a diagnosis that has become ubiquitous in the United States. The number of children diagnosed with this disorder increases every year (CDC, 2023). Despite this rapid growth, researchers still struggle to identify the etiology of most cases (NIH, 2024). It is apparent that this is a heterogenous disorder with unique neurological contributions (Lombardo et al., 2019; Vicedo, 2023). In addition to the commonly cited differences of social, communication and behavior, up to 88% of all people with autism also have motor impairments (American Psychiatric Association, 2013; Kangarani-Farahani et al., 2023). These impairments impact autistic individuals' abilities to perform daily living skills (Travers et al., 2022). As such, occupational therapy practitioners (OTPs) are commonly called upon to work with people with autism (Benevides et al., 2022).

Despite the widespread presence of motor impairments, the evidence-based to support interventions to improve motor skills is meager in the occupational therapy (OT) field. Studies in and out of the field lack robust sample sizes and often fail to identify a proposed mechanism of action. To complicate matters, the unique neurology of the autistic brain may alter how an individual responds to interventions. Poor neuromodulation may negatively impact an autistic child's ability to respond to an OT intervention (Dicarlo & Wallace, 2022; Friedman et al., 2006; Karvat & Kimchi, 2014; Yoo et al., 2007).

With the advent of precision medicine, OT has the opportunity to contribute to the development of person-centered interventions that maximize an individual's potential to participate in daily living skills (AOTA, 2021). However, a precision intervention model is currently out of reach for OTPs working with children with autism. Researchers must first identify observable characteristics that are predictive of how an individual will respond to intervention. The first step in this process is discovering phenotypes, or personal profiles, that assist the OTP in determining if a proposed intervention will be impactful for a client. The first phase of this program sets out to achieve this objective by observing how psychometrics and biometrics measurements align. Once patterns have been identified, researchers may be able to identify which key ingredients needed to be included in an intervention to make it effective for a specific phenotype.

One intervention that is promising for amplifying the impact of motor skill learning techniques is vagal nerve stimulation (VNS). VNS, and its less invasive counterpart transcutaneous vagal nerve stimulation (tVNS) are currently being deployed for improving motor skills in stroke patients (Dawson et al., 2021; Liu et al., 2022). The proposed mechanism of action is the neuroplastic environment created when the vagus nerve is stimulated. Autism researchers have suggested that this same mechanism of action may make it a useful adjunct intervention for people with autism (Engineer et al., 2017; Jin & Kong, 2016; van Hoorn et al., 2019). If phase one reveals that poor neuromodulation aligns with motor skill delays, then an intervention targeting both neuromodulation and physical skills may be impactful (Bowles et al., 2022; Keute & Gharabaghi, 2021). Phases two and three of this program set out to further explore these concepts.

The field of occupational therapy has always believed in the uniqueness of each client we serve (AOTA, n.d.). We assess each client as a whole, creating comprehensive interventions to empower our clients in living the life they desire (AOTA, 2020). Precision intervention is the next step in our evolution. This program represents first steps towards this endeavor.

APPENDIX A – Teaching Plan

The teaching plan example in Table A1 illustrates how occupational therapy practitioners will be trained to utilize the manualized intervention planned for deployment in phases two and three of this program.

Table A1

Teaching Plan Example for Manualized Intervention

Overall Learning Goal: Occupational therapy practitioners (OTPs) will demonstrate the correct use of the decision tree for identifying feedback hierarchy during motor training tasks.

Specific Learning Objective 1: Following completion of reading materials, OTPs will correctly recall the three types of feedback with 80% or higher proficiency.

Learning activities and supporting learning theories:	Method of teaching	Time allotted	Resources	Method of evaluation
OTPs will be provided with a handout to read on motor learning theory and the feedback hierarchy approach of most to least prompting (MTL). The theories guiding this approach are the cognitive learning theory and the theory of andragogy. The cognitive theory emphasizes mental functions and information processing (Nguyen, 2020). Andragogy emphasizes the autonomy of adult learners (Hayes, 2016). The OTPs in this program are volunteers who are interested in pursuing additional learning in this area. This activity allows for autonomous learning of new information.	Asynchronous learning: learners will be provided with an information handout, review the handout, complete the quiz, and be provided with immediate results.	15–30 minutes depending on the learner (self-paced)	Handout and online quiz	Online quiz

Specific Learning Objective 2: Following a presentation about the manualized decision tree for identifying feedback hierarchy, OTPs will correctly identify appropriate level of feedback given client scenarios with 80% or higher accuracy.				
Learning activities and supporting learning theories:	Method of teaching	Time	Resources	Method of evaluation
OTPs will participate in an interactive lecture/ role play forum where the manualized plan will be presented and they will actively work through client scenarios to identify which feedback level to use for which scenarios. The theory guiding this approach is the social cognitive theory (SCT) which emphasizes reciprocal determinism (LaMorte, 2022). This activity discusses how to implement the intervention into a therapy session and promotes learning engagement.	Interactive lecture: learners will be provided with visual supports (PowerPoint and handout) to go along with the lecture and interaction will be facilitated through group problem solving.	60 minutes	PowerPoint, handout, tracking log, classroom	Tracking log to be provided to participants to self report accuracy.

Specific Learning Objective 3: Following a demonstration of a treatment session, OTPs will accurately identify if the feedback provided followed the manualized approach with 80% or higher accuracy.				
Learning activities and supporting learning theories:	Method of teaching	Time allotted	Resources	Method of evaluation
Participants will watch videos of the intervention being provided to clients. They will indicate if the treating therapist utilized the correct feedback level based on the client's performance in the session. The theory guiding this activity is the SCT. The SCT emphasizes observation learning and self efficacy. This activity provides peer modeling and supports gradual skill development.	Asynchronous video review: learners will be provided with the feedback hierarchy decision tree and videos of the intervention being applied.	30 minutes	Videos of treatment and feedback hierarchy decision tree	Decision trees will be graded for accuracy.

Specific Learning Objective 4: During a therapy session, OTPs will accurately apply the correct feedback level to the client based on the client's performance level, with 80% or higher accuracy.				
Learning activities and supporting learning theories:	Method of teaching	Time allotted	Resources	Method of evaluation
Participants will practice using the decision tree with actual clients. Sessions will be videotaped and reviewed as a group. The SCT theory guides this activity by allowing participants to learn through observation and analyzing their peers. It also relies on the Experiential Learning theory. This theory emphasizes reflective observation and active experimentation as key elements of learning (Institute for Experiential Learning, n.d.).	Asynchronous therapy sessions, video recorded. Synchronous video review in a group format.	60 minutes	Practice clients, recording devices, videos of sessions, decision trees, classroom	Videos will be reviewed for accuracy. Reflective observation responses will be tracked for accuracy.

APPENDIX B – Budget Details for Phase One-Three

The line item details for the budgets of phases one through three are detailed in Figure B1.

Figure B1

Budget Details for Phase One-Three

PHASE ONE				
Personnel				
Primary Investigator				
Activity	**Hours Required**	**Amount**	**Donor Amount**	**In kind Amount**
IRB proposal and defense	6	552	0	552
Grant writing	12	1104	0	1104
Staff training on evaluation procedures	3	276	0	276
Staff training on admission procedures	3	276	0	276
Volunteer training on data entry	3	276	0	276
Report writing	80	7360	7360	0
Report revisions and editing	80	7360	0	7360
Total Amounts	187	17204	7360	9844
Therapy Staff				
Activity	**Hours Required**	**Amount**	**Donor Amount**	**In kind Amount**
Evaluations (n= 50; 2hr/ evaluation)	100	6800	6800	0
Total Hours	100	6800	6800	0
Total Amount	200	$ 13,600	$ 13,600	$ -
Research Staff				
Activity	**Hours Required**	**Amount**	**Donor Amount**	**In kind Amount**
Research Administration (n= 3% of total project hours)	9	1818	1818	0
Research Data Analysis (n= 3% of total project hours)	9	1818	0	1818
Total Amount	18	$ 3,636	$ 1,818	$ 1,818

Category	Amount per Item	Amount	Donor Amount	In kind Amount
		Outcome Measures and Participant Fees		
Category	**Amount per Item**	**Amount**	**Donor Amount**	**In kind Amount**
Oura ring n=25	350	8750	8750	0
iPads n=25	325	8125	4225	3900
BOT-2 protocol sheets n=2 packages	125	250	250	0
BOT-2 kit	1198	1198	0	1197.5
GARS-3 manual and protocol sheets	250	250	250	0
Participant Reimbursement	100	2500	2500	0
Total Amount	$ 2,348	$ 21,073	$ 15,975	$ 5,098
		Dissemination		
Category	**Amount per Item**	**Amount**	**Donor Amount**	**In kind Amount**
American Occupational Therapy Association (AOTA) annual conference attendance and travel	2600	2600	0	2600
International Society for Autism Research (INSAR) annual conference attendance and travel	3200	3200	3200	0
Video script writing and recording (n=5 videos)	184	920	0	920
Video design and editing (n=5)	184	920	920	0
Total Amount	$ 6,168	$ 7,640	$ 4,120	$ 3,520
Total Amount for Phase One	--	$ 63,153	$ 42,873	$ 20,280

PHASE TWO				
Personnel				
Primary Investigator				
Activity	**Hours Required**	**Amount**	**Donor Amount**	**In kind Amount**
IRB proposal and defense	6	552	0	552
Grant writing	12	1104	0	1104
Staff training on evaluation procedures	3	276	0	276
Staff training on admission procedures	3	276	0	276
Volunteer training on data entry	3	276	0	276
Staff training on intervention	3	276	0	276
Student training on video review	3	276	0	276
Weekly meetings to ensure fidelity to intervention (weeks n=24)	24	2208	0	2208
Report writing	80	7360	7360	0
Report writing revisions and editing	80	7360	0	7360
Total Amounts	217	$ 19,964	$ 7,360	$ 12,604
Activity	**Hours Required**	**Amount**	**Donor Amount**	**In kind Amount**
Evaluations (participants n=5; evaluations n=2/participant; time to complete 1 evaluation n= 2hours)	20	1360	1360	0
Weekly meetings to ensure fidelity to intervention (practitioners n=5; weeks n=24)	120	8160	0	8160
Baseline (A) (n= 4 weeks; 1 hour per week)	20	1360	1360	0
Intervention (B, C) (n=8 weeks; sessions n=16/participant)	80	5440	5440	0
Return to Baseline (A) (n=4 weeks; 1 hour per week + 30 additional min. final week)	23	1564	1564	0
Total Amount	263	$ 17,884	$ 9,724	$ 8,160
Research Staff				
Activity	**Hours Required**	**Amount**	**Donor Amount**	**In kind Amount**
Research Administration (n= 3% of total project hours)	14	2828	2828	0
Research Data Analysis (n= 3% of total project hours)	14	2828	0	2828
Total Amount	28	$ 5,656	$ 2,828	$ 2,828

		Outcome Measures and Participant Fees		
Category	**Amount per item**	**Amount**	**Donor Amount**	**In kind Amount**
Oura ring (n=5)	350	1750	0	1750
iPads (n=5)	325	1625	0	1625
BOT-2 protocol sheets (n=10)	5	50	50	0
BOT-2 kit	1198	1198	0	1198
GARS-3 protocol sheets (n= 10)	2	20	20	0
GARS-3 manual	250	250	0	250
Participant Reimbursement	200	1000	1000	0
Total Amount	$ 2,330	$ 5,893	$ 1,070	$ 4,823
		Clinical Supplies		
Category	**Amount per item**	**Amount**	**Donor Amount**	**In kind Amount**
tVNS units (n=5)	652	3260	3260	0
Play Supplies (n=$15/session)	15	360	0	360
Total Amount	$ 667	$ 3,620	$ 3,260	$ 360
		Dissemination		
Category	**Amount per item**	**Amount**	**Donor Amount**	**In kind Amount**
American Occupational Therapy Association (AOTA) annual conference attendance and travel	2600	2600	0	2600
International Society for Autism Research (INSAR) annual conference attendance and travel	3200	3200	3200	0
Video script writing and recording (n=5 videos)	184	920	0	920
Video design and editing (n=5 videos)	184	920	920	0
Total Amount	$ 6,168	$ 7,640	$ 4,120	$ 3,520
Total Amount for Phase Two	--	$ 60,657	$ 28,362	$ 32,295

APPENDIX C – Executive Summary

Introduction

Autism is a neurodevelopmental disorder that is pervasive in the United States. In 2000, the rate of autism was one in 150 children. Twenty years later, it is diagnosed in one in 36 children (CDC, 2024). This widespread developmental disorder is characterized by repetitive and restricted interests and differences in social and communication skills (NIH, 2024a). Moreover, motor skill deficits are seen in most autistic individuals resulting in impaired ability to perform daily living skills (Bhat, 2020; Ozboke et al., 2021). These diminished motor abilities can be explained through the lens of neurology. The parts of the brain that are responsible for motor control and motor refinement develop differently in autistic people when compared to others without autism. This difference in neurology can complicate attempts to remediate motor skills.

Occupational therapy practitioners (OTPs) are holistic healthcare professionals who commonly work with people with autism to improve their motor skills (Benevides et al., 2022; Yingling & Bell, 2020). Occupational therapy (OT) emphasizes supporting people with activities of daily living (AOTA, n.d.). There is a focus in the field on improving participation in daily activities. Motor skills are needed to successfully participate in many facets of life, including leisure activities and activities of daily living (Kaur et al, 2018; Travers et al., 2017). Unfortunately, the OT literature on motor skill interventions is sparse. Over the last decade, only 13 studies have been published in the OT literature investigating the effectiveness of motor skill intervention. Other professionals, like physical therapists or physical education teachers, also address motor skills in autism. The broader publications on motor skill intervention are more robust. However, in its entirety, the literature lacks a consensus on what intervention is most effective, why it is effective, and who would benefit from it. This may result in inefficient interventions, requiring more therapy to achieve smaller gains.

Project Overview

This project seeks to take the first steps towards developing interventions specifically designed for the unique individual receiving the intervention. This approach is borrowed from other fields and is called “precision medicine” or “precision intervention." Precision medicine is an emerging field based on the newfound knowledge of the genome (NIH, 2023). The genome is all the genetic material in a person. By identifying the specific genetic composition of an individual, interventions can be customized for that person. The field of precision medicine is still in the early stages. In the autism domain, researchers have been working to identify specific genes responsible for autism (Matta et al., 2022). Although much progress has been made, the manifestation of precision medicine in autism is still just a dream.

Precision intervention does not solely rely on unraveling the genomic fingerprint of autism. Other biomarkers can be considered when attempting to develop individualized care. This project will look at specific biometrics that relate to motor skill development in children with autism. Although it is possible to peer into the brains of children using advanced technology, such as functional Magnetic Resonance Imaging (fMRI) or Diffusion Tensor Imaging (DTI), these procedures can be difficult for children to tolerate. Phase one of this project will identify noninvasive measures of neurobiological functioning. In addition, motor skill measurements will be gathered and analyzed. By identifying how motor skills relate to specific biometrics, a motor phenotype, or profile, can be developed to guide intervention.

From there, phase two explores the effectiveness of an intervention that partners a biological intervention with traditional motor rehabilitation techniques. The biological intervention is called transcutaneous vagus nerve stimulation (tVNS). The vagus nerve is a very important nerve that connects the body and its organs to the brain. It plays a crucial role in regulating the heart, the breath, and the digestive system. It exerts this control by regulating, or modulating, various neurochemicals. Interestingly, many of the neurochemicals that the vagus nerve regulates are important for motor learning. Furthermore, people with autism have irregularities with these specific neurochemicals. The vagus nerve can be activated using tVNS. Research has shown that by stimulating the vagus nerve, some people experience improvements in motor learning (Morrison et al., 2019). Phase two of this project is a feasibility study to determine if children with autism will tolerate tVNS followed by traditional OT intervention to build motor skills. The information gained in phase one about motor phenotypes will help to guide the recruitment of individuals who are most likely to benefit from the intervention. Phase three will take the information learned from phases one and two and apply it to a widescale, randomized controlled trial.

Key Findings

Neurological Differences

This project is in its infancy. Findings are derived from the extensive literature review that was undertaken to develop the methodology for each phase. The results reveal that autistic people have brains that develop uniquely. There are differences in the way the brain looks (morphology), the way the cells in the brain look (cytoarchitecture), and the way brain cells are connected (neural connectivity) (Dicarlo & Wallace 2022; Fatemi et al., 2012; Friedman et al., 2006; Xu et al., 2020). There are also differences in the brain chemicals (neurotransmitters) (Bast et al., 2018). All of these differences have a cascading impact on development and help to explain why motor skill impairments are so widespread in this population.

Motor Differences

A number of studies have identified motor skill differences in people with autism (Kaur et al., 2018; Linke et al., 2020; Posar & Visconti, 2022; Tse et al., 2022). Impairments in fine motor and gross motor skills have been described (Volkan-Yazici et al., 2018). These deficits present early in life and do not resolve with age (Lidstone & Mostofsky, 2021). In other words, children do not simply grow out of the delays. Research has shown that motor deficiencies can result in difficulty with completing everyday tasks like getting dressed or preparing a meal (Travers et al., 2017). Despite these important implications, motor skill interventions are not well developed.

Motor Interventions

A search of the literature reveals that there is little consensus on who should implement motor interventions and what those interventions should be. Various professionals, including physical therapists, occupational therapists, physical education teachers, and even parents have been utilized in studies to provide the intervention. In addition, many different approaches have been used in an attempt to improve motor skills in autistic children. Examples include interventions that use animals, exercise, aquatics, sports, technology, or music (Bremer et al., 2016; De Milander et al., 2016; Friedman et al., 2023; Guest et al., 2017; Hilton et al., 2014; Marzouki et al., 2022). No single approach has been established as superior to others. To further complicate matters, the amount of intervention needed to obtain significant gains has not been well established. Studies vary from 3 hours to 36 hours or more of intervention.

One explanation for this lack of consensus is that most studies do not identify the key ingredients of the intervention. Key ingredients are the essential components of an intervention that are integral to its implementation. In order to identify key ingredients, a researcher must have a hypothesis of the mechanism of action. The mechanism of action is the theory of why a key ingredient would be effective. Because most intervention studies do not include this valuable information, it is difficult to build a knowledge base on which to build consensus.

Neurological Interventions

Research has established that stimulating the vagus nerve can effectively improve motor skills (Dawson et al., 2021). The mechanism of action for this intervention relates to the function of the vagus nerve. The vagus nerve conveys information from the body to the brain (Yamakawa et al, 2015). The parts of the brain that the vagus nerve “talks” to are important for motor learning. By activating the vagus nerve, the brain is primed for motor learning (Hulsey et al., 2019). Therefore, vagus nerve stimulation should be considered a key ingredient for motor skill interventions targeting biological changes (Engineer et al., 2017).

Recommendations

The field of occupational therapy is well-suited for developing precision interventions to improve motor skills in children with autism. The profession's emphasis on improving participation by considering the physical and biological attributes of the client is a good match for the principles of precision intervention (AOTA, 2020). The profession should increase its efforts to produce high-quality intervention studies on motor skills in children with autism. Furthermore, the profession should consider adjunct interventions to amplify traditional approaches.

Conclusion

Motor skill deficits are a pervasive problem for people with autism with cascading impacts on participation in everyday activities. OTPs are commonly sought to support autistic people in improving their participation (Monz et al., 2019). Unfortunately, there is no clear consensus in the literature to inform evidence-based practice when addressing motor skills in this population. This project seeks to establish a biological and motor skill profile in children with autism to inform an adjunctive intervention that includes biological and motor targets. Through these efforts, the future of precision intervention and occupational therapy in autism looks optimistic, offering hope for more effective and personalized support that empowers individuals.

APPENDIX D – Fact Sheet

BOSTON UNIVERSITY

Innovative Interventions

Neuromodulation to Enhance Motor Learning in Autism

The Problem

Between 35%-88% of autistic people have motor impairments (Kangarani-Farahani et al., 2023)

Motor deficits negatively impact independence with daily living skills (Travers et al., 2017).

Autistic brains are neurologically unique and require a unique approach (Bharath et al., 2019).

Current OT practice does not consider how neurology may impact physiology which may result in less effective interventions.

What Occupational Therapy (OT) is Doing Now

There is very little OT research investigating motor interventions. In the last 10 years, only 13 OT studies have been conducted in this area. There is currently no consensus on the best approach to intervention or the optimal amount of therapy needed. A wide range of interventions have been utilized with the duration of treatment ranging from 3-30 hours. The quality of the studies has generally been low and studies rarely cite the mechanism of action or theory guiding the intervention.

How Motor Skills Develop

Motor Learning is modulated by several key neurotransmitters (Matur & Öge, 2017). Norepinephrine and acetylcholine prime the brain for learning by facilitating alertness and attention. When the approximate motor action is executed, dopamine is released. Then, motor memories are incorporated during sleep.

Neuromodulation

The vagus nerve plays a key role in modulating the neurotransmitters involved in motor skill learning. Autistic people commonly have low vagal tone, suggesting poor neuromodulation (Matsushima et al., 2016). By enhancing the function of the vagus nerve, motor learning may be amplified.

Michele Alaniz, BCP, OTR/L

Precision Intervention

The vision of this program is to develop a precision intervention for autism treatment. Precision medicine is when treatment is tailored for an individual based on their phenotype. A phenotype is a personal profile based on factors such as biology, genetics, and other observable traits. Phenotypes allow for more targeted interventions based on an individual's specific profile. The field of occupational therapy is poised to pioneer innovative interventions in this area of development. This will, in turn, further support occupational therapy as an evidence-based, fundable service. This program investigates how biometrics correlate with psychometrics in children with autism, establishing a motor phenotype. From there, it tests the effectiveness of an intervention that targets both biological and physical factors. Findings will support clinical practice.

Funding: Grant funding for all phases of the program	Access: Participants will be recruited through the host hospital for the study

Phases of the Program

Phase One

Correlative study to establish a motor phenotype using biometrics and psychometrics. Biometrics will be collected related to vagal nerve function including sleep, heart rate variability, respiratory rate and indirect measures of dopamine and norepinephrine. Psychometrics include fundamental motor skills.

Phase Two

Single subject design to establish the feasibility of vagal nerve stimulation delivered via an external clip on the ear (tVNS), followed by motor skill training. Biometrics and psychometrics will be gathered to determine preliminary effectiveness.

Phase Three

Randomized controlled trial to test the effectiveness of using a manualized motor training intervention partnered with tVNS to promote neuromodulation in autistic children.

			
Psychometrics	Biometrics	Sleep	tVNS

Additional Information

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