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The Impact of Early Intervention on Motor Outcomes in Infants with Cerebral Palsy: A Longitudinal Study with Advanced Neuroimaging Correlates in Surabaya, Indonesia

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A B S T R A C T

Introduction: Cerebral palsy (CP) is a prevalent neurodevelopmental disorder affecting motor function in children. Early intervention (EI) has been shown to improve motor outcomes in infants with CP, but the underlying neural mechanisms remain poorly understood. This longitudinal study investigated the impact of EI on motor outcomes and its association with neuroimaging correlates in infants with CP in Surabaya, Indonesia. **Methods:** We recruited 60 infants diagnosed with CP aged 6-18 months in Surabaya, Indonesia. Participants were randomly assigned to either an EI group receiving 6 months of individualized, home-based intervention or a control group receiving standard care. Motor function was assessed using the Gross Motor Function Measure (GMFM-88) at baseline, 6 months, and 12 months. Advanced neuroimaging techniques, including diffusion tensor imaging (DTI) and functional magnetic resonance imaging (fMRI), were used to assess brain structure and function at baseline and 12 months. **Results:** Infants in the EI group demonstrated significantly greater improvements in GMFM-88 scores compared to the control group at 6 and 12 months ($p < 0.05$). DTI revealed increased fractional anisotropy (FA) in the corticospinal tract and corpus callosum in the EI group at 12 months, indicating improved white matter integrity. fMRI showed increased functional connectivity in motor networks in the EI group compared to the control group at 12 months. **Conclusion:** Early intervention significantly improved motor outcomes in infants with CP in Surabaya, Indonesia. These improvements were associated with enhanced white matter integrity and functional connectivity in motor-related brain regions. Our findings highlight the importance of early intervention in promoting neuroplasticity and improving motor function in infants with CP.

1. Introduction

Cerebral palsy (CP) is a prevalent neurodevelopmental disorder that affects movement and posture, presenting a significant challenge to children and their families worldwide. Characterized by a spectrum of motor impairments, including spasticity, muscle weakness, and coordination difficulties, CP arises from damage to the developing brain. This non-progressive condition can significantly impact a child's functional independence, overall well-being, and quality of life. The estimated prevalence of CP is 2-3 per 1000 live births globally, making it the most common cause of childhood physical disability. The impact of CP extends beyond the physical realm, often influencing cognitive, communicative, and socio-emotional development. The heterogeneous nature of CP presents unique challenges in diagnosis, management, and intervention, underscoring the need for comprehensive and individualized approaches to care.[1-3]

Early intervention (EI) has emerged as a cornerstone in the management of CP, offering a range of therapeutic and educational interventions aimed at maximizing the developmental potential of infants and young children. The philosophy of EI is rooted in the concept of neuroplasticity, the brain's ability to reorganize and adapt in response to experiences, particularly during the early years of development. By providing targeted interventions during this critical period, EI aims to promote motor development, prevent secondary complications, and enhance overall well-being. Numerous studies have documented the positive effects of EI on motor outcomes in infants with CP. These interventions often involve a combination of physical therapy, occupational therapy, speech therapy, and early childhood education, tailored to the specific needs of each child. The goals of EI are multifaceted and include improving muscle strength and coordination, enhancing functional mobility, promoting communication and social interaction, and fostering cognitive development.[4-7]

Despite the growing body of evidence supporting the benefits of EI, the underlying neural mechanisms driving these improvements remain an area of active investigation. Advanced neuroimaging techniques, such as diffusion tensor imaging (DTI) and functional magnetic resonance imaging (fMRI), have provided valuable tools for exploring brain structure and function in children with CP. DTI offers insights into the microstructural properties of white matter, the brain's communication pathways, while fMRI allows for the examination of brain activity patterns.[8-10] This study aimed to investigate the impact of EI on motor outcomes in infants with CP and to explore the relationship between these improvements and changes in neuroimaging correlates.

2. Methods

This longitudinal study was conducted in Surabaya, Indonesia, a bustling metropolis located on the eastern coast of Java Island. Surabaya, known for its rich cultural heritage and vibrant economy, is also a major center for healthcare in the region. The study was conducted at a leading private hospital in Surabaya, renowned for its advanced medical facilities and commitment to providing comprehensive care to children with neurological conditions. The hospital's Department of Child Neurology served as the primary recruitment site, offering access to a diverse population of infants diagnosed with CP. The decision to conduct the study in Surabaya was driven by several factors, including the high prevalence of CP in Indonesia, the hospital's expertise in pediatric neurology, and the availability of advanced neuroimaging facilities. The longitudinal design of the study allowed for the examination of changes in motor outcomes and neuroimaging correlates over time, providing valuable insights into the dynamic interplay between brain development and intervention. The study adhered to the ethical principles outlined in the Declaration of Helsinki and was approved by the hospital's Institutional Review Board.

Participants were recruited from the Department of Child Neurology at the Private Hospital in Surabaya, Indonesia. The inclusion criteria were as follows; Confirmed diagnosis of CP by a pediatric neurologist; Age between 6 and 18 months; No other neurological or medical conditions; No prior participation in EI programs. The exclusion criteria were as follows; Severe cognitive impairment; Visual or hearing impairment; Contraindications to MRI. These criteria were carefully selected to ensure a homogenous study population and to minimize the influence of confounding factors on the study outcomes. The age range of 6 to 18 months was chosen to capture the critical period of early brain development when neuroplasticity is at its peak.

Parents or legal guardians of infants who met the inclusion criteria were approached by the study coordinator during their visit to the Department of Child Neurology. The study coordinator explained the study objectives, procedures, and potential benefits and risks to the parents. Written informed consent was obtained from all parents or legal guardians prior to enrollment in the study. The informed consent process emphasized the voluntary nature of participation and the right to withdraw from the study at any time without penalty.

Following informed consent, participants were randomly assigned to either the EI group or the control group using a computer-generated randomization sequence. The randomization process ensured that each participant had an equal chance of being assigned to either group, minimizing the risk of selection bias. The trained physiotherapists responsible for administering the GMFM-88 assessments were blinded to group allocation. This blinding procedure was implemented to prevent assessor bias from influencing the motor outcome measurements.

The EI group received 6 months of individualized, home-based intervention, consisting of 3 sessions per week, each lasting 1 hour. The intervention was delivered by trained therapists with expertise in pediatric rehabilitation. These therapists underwent rigorous training to ensure fidelity to the intervention protocol. The intervention program was grounded in the principles of neurodevelopmental therapy (NDT) and sensory integration therapy, both widely recognized approaches in the field of pediatric rehabilitation. NDT focuses on facilitating normal movement patterns and promoting functional skills, while sensory integration therapy aims to enhance the processing of sensory information. The intervention program was tailored to each infant's specific needs and abilities, taking into account their motor impairments, developmental stage, and individual preferences. The home-based nature of the intervention allowed for integration of therapeutic activities into the child's natural environment, promoting generalization of skills and active involvement of parents or caregivers. The control group received standard care, which included regular check-ups with their pediatrician and access to community-based services. Standard care typically involves monitoring of growth and development, immunizations, and management of any medical conditions.

Motor function was assessed using the Gross Motor Function Measure (GMFM-88), a standardized and validated observational instrument designed to evaluate gross motor skills in children with CP. The GMFM-88 consists of 88 items assessing various dimensions of gross motor function, including lying and rolling, sitting, crawling and kneeling, standing, and walking, running, and jumping. Each item on the GMFM-88 is scored on a 4-point scale, ranging from 0 to 3, with higher scores indicating better motor function. The GMFM-88 was administered at baseline, 6 months, and 12 months by trained physiotherapists who were blinded to group allocation. All participants underwent MRI scans at baseline and 12 months using a 3T MRI scanner. The MRI scans were performed by experienced radiographers following standardized protocols. DTI data were acquired using a single-shot echo-planar imaging sequence with 30 diffusion directions. DTI is a neuroimaging technique that provides information about the microstructural properties of white matter, the brain's communication pathways. Fractional anisotropy (FA) values were calculated for the corticospinal tract and corpus callosum, which are major white matter pathways involved in motor control. FA is a measure of the directionality of water diffusion in white matter, reflecting the integrity and organization of axons. fMRI data were acquired using a blood oxygen level-dependent (BOLD) contrast sequence during a resting-state paradigm. fMRI is a neuroimaging technique that measures brain activity by detecting changes in blood flow. Functional connectivity was assessed between motor-related brain regions, including the primary motor cortex, premotor cortex, and supplementary motor area. Functional connectivity refers to the temporal correlation of activity between different brain regions, reflecting the integration of neural processes.

Data were analyzed using SPSS software (version 25). Descriptive statistics were used to summarize participant characteristics and outcome measures. Repeated measures ANOVA was used to compare changes in GMFM-88 scores over time between the EI and control groups. Independent t-tests were used to compare FA values and functional connectivity measures between the two groups at 12 months. Pearson correlation analyses were used to examine the relationship between changes in GMFM-88 scores and neuroimaging measures. Statistical significance was set at $p < 0.05$.

3. Results

Table 1 presents the baseline characteristics of the 60 infants with Cerebral Palsy (CP) enrolled in the study, divided into two groups: the Early Intervention (EI) group and the Control group; Age: The average age of the infants was roughly 11 months in both groups. The ages ranged from 6 to 18 months, capturing a key period for early brain development. There was no statistically significant difference in age between the two groups (p=0.52), suggesting that age is unlikely to be a confounding factor in the study; Gender: Both groups had a similar proportion of males and females. Approximately 60% of the EI group and 53% of the Control group were male. The difference in gender distribution between the groups was not statistically significant (p=0.61); CP Subtype: The most common type of CP in both groups was spastic CP, affecting 70% of the participants in each group. Dyskinetic and mixed CP subtypes were less common. The distribution of CP subtypes was identical in both groups. This ensures that any observed differences in outcomes are less likely to be attributed to variations in CP type; Gross Motor Function Measure (GMFM-88) Score: The GMFM-88 is a standardized test used to assess gross motor skills in children with CP. At baseline, both groups had similar average GMFM-88 scores (EI group: 28.5, Control group: 27.8). The difference was not statistically significant (p=0.78), indicating that the groups had comparable motor function at the start of the study. This is crucial for a randomized controlled trial, as it ensures that the groups are starting from a similar point, allowing for a fair comparison of the effects of the intervention.

Table 1. Participant characteristics.

Characteristic	**Early Intervention Group (n=30)**	**Control Group (n=30)**	**p-value**
Age (months)			
Mean ± SD	11.5 ± 3.1	10.9 ± 3.7	0.52
Range	6 - 18	6 - 18	
Gender			
Male	18 (60%)	16 (53.3%)	0.61
Female	12 (40%)	14 (46.7%)	
CP subtype			
Spastic	21 (70%)	21 (70%)	1.00
Dyskinetic	6 (20%)	6 (20%)	
Mixed	3 (10%)	3 (10%)	
Gross Motor Function Measure (GMFM-88) score			
Baseline (mean ± SD)	28.5 ± 12.3	27.8 ± 11.8	0.78

Table 2 presents the changes in gross motor function, as measured by the GMFM-88, in both the Early Intervention (EI) and Control groups over time; Improvements in Motor Function: Both groups showed improvements in their GMFM-88 scores from baseline to 6 months and from baseline to 12 months. This is expected, as children with CP generally experience some degree of motor development over time, even without intervention; Greater Improvements in the EI Group: The EI group demonstrated significantly greater improvements in GMFM-88 scores compared to the Control group at both 6 months (p=0.02) and 12 months (p=0.01). This suggests that the EI program had a positive impact on motor development above and beyond the natural progression of motor skills in children with CP; Sustained Improvement in the EI Group: The EI group also showed continued improvement in motor function from 6 months to 12 months (p=0.04), while the improvement in the Control group during this period was not statistically significant (p=0.12). This indicates that the benefits of EI were not only immediate but also sustained over time.

Table 2. Motor outcomes (GMFM-88 Scores).

Group	**Baseline (Mean ± SD)**	**6 Months (Mean ± SD)**	**12 Months (Mean ± SD)**	**p-value (Baseline vs. 6 Months)**	**p-value (Baseline vs. 12 Months)**	**p-value (6 Months vs. 12 Months)**
Early Intervention	28.5 ± 12.3	38.2 ± 11.8	41.0 ± 11.1	0.02	0.01	0.04
Control	27.8 ± 11.8	32.5 ± 11.2	34.1 ± 10.5	0.08	0.06	0.12

Table 3 provides insights into the neuroimaging correlates of motor function in infants with CP, comparing the Early Intervention (EI) group and the Control group. The table focuses on two key neuroimaging measures: Fractional Anisotropy (FA) and Functional Connectivity; Fractional Anisotropy (FA): At baseline, there was no significant difference in FA values of the corticospinal tract between the two groups. However, at 12 months, the EI group showed significantly higher FA values in this tract compared to the Control group (p=0.03). The corticospinal tract is a crucial pathway for voluntary motor control, and higher FA values indicate better organization and integrity of this pathway. This finding suggests that EI may promote the development and maturation of the corticospinal tract in infants with CP. Similar to the corticospinal tract, there was no significant difference in FA values of the corpus callosum between the groups at baseline. However, at 12 months, the EI group showed significantly higher FA values in the corpus callosum compared to the Control group (p=0.04). The corpus callosum is the major pathway connecting the two hemispheres of the brain, and its integrity is important for coordinating movement and integrating information from both sides of the body. This finding suggests that EI may also enhance the development of the corpus callosum in infants with CP; Functional Connectivity (Resting-state fMRI): At baseline, there was no significant difference in functional connectivity between the primary motor cortex and premotor cortex between the two groups. However, at 12 months, the EI group showed significantly stronger functional connectivity between these two regions compared to the Control group (p=0.02). The premotor cortex plays a role in planning and preparing for movement, and its strong connectivity with the primary motor cortex is essential for efficient motor control. Similarly, there was no significant difference in functional connectivity between the primary motor cortex and supplementary motor area at baseline. However, at 12 months, the EI group showed significantly stronger functional connectivity between these regions compared to the Control group (p=0.04). The supplementary motor area is involved in higher-level motor planning and sequencing of movements.

Table 3. Neuroimaging correlates.

Measure	Early Intervention Group (n=30)	Control Group (n=30)	p-value (EI vs. Control)
Fractional Anisotropy (FA)			
Corticospinal Tract (Baseline, Mean ± SD)	0.45 ± 0.08	0.43 ± 0.07	0.25
Corticospinal Tract (12 Months, Mean ± SD)	0.52 ± 0.09	0.46 ± 0.08	0.03
Corpus Callosum (Baseline, Mean ± SD)	0.38 ± 0.06	0.37 ± 0.05	0.31
Corpus Callosum (12 Months, Mean ± SD)	0.44 ± 0.07	0.40 ± 0.06	0.04
Functional Connectivity (Resting-state fMRI)			
Primary Motor Cortex - Premotor Cortex (Baseline, Mean ± SD)	0.25 ± 0.10	0.23 ± 0.09	0.38
Primary Motor Cortex - Premotor Cortex (12 Months, Mean ± SD)	0.38 ± 0.12	0.28 ± 0.11	0.02
Primary Motor Cortex - Supplementary Motor Area (Baseline, Mean ± SD)	0.30 ± 0.11	0.28 ± 0.10	0.42
Primary Motor Cortex - Supplementary Motor Area (12 Months, Mean ± SD)	0.42 ± 0.13	0.33 ± 0.12	0.04

Table 4 presents the correlations between changes in motor function (GMFM-88 scores) and neuroimaging measures in infants with CP who participated in the study. There were significant positive correlations between changes in GMFM-88 scores and all three neuroimaging measures: FA in the corticospinal tract ($r = 0.45$, $p < 0.05$), FA in the corpus callosum ($r = 0.38$, $p < 0.05$), and functional connectivity between the primary motor cortex and premotor cortex ($r = 0.32$, $p < 0.05$). This indicates that greater improvements in motor function were associated with greater increases in white matter integrity in key motor pathways and stronger functional connectivity between motor-related brain regions. The correlations between changes in GMFM-88 scores and FA values were stronger than the correlation with functional connectivity. This suggests that white matter integrity may be a more robust predictor of motor improvements in infants with CP. There were also significant positive correlations between the neuroimaging measures themselves. FA in the corticospinal tract was strongly correlated with FA in the corpus callosum ($r = 0.65$, $p < 0.01$), suggesting that these two white matter pathways develop in concert. Both FA measures were also significantly correlated with functional connectivity between the primary motor cortex and premotor cortex ($r = 0.55$ and $r = 0.48$, respectively, $p < 0.01$). This indicates that improvements in white matter integrity are associated with stronger functional connectivity in the motor network.

Table 4. Correlation analysis.

Measure	Change in GMFM-88 Score (Baseline to 12 Months)	FA Corticospinal Tract (12 Months)	FA Corpus Callosum (12 Months)	Functional Connectivity (Primary Motor Cortex - Premotor Cortex, 12 Months)
Change in GMFM-88 Score (Baseline to 12 Months)	1.00	-	-	-
FA Corticospinal Tract (12 Months)	0.45*	1.00	-	-
FA Corpus Callosum (12 Months)	0.38*	0.65**	1.00	-
Functional Connectivity (Primary Motor Cortex - Premotor Cortex, 12 Months)	0.32*	0.55**	0.48**	1.00

*p < 0.05, ** p < 0.01.

4. Discussion

Our study unequivocally demonstrates the profound and enduring impact of early intervention (EI) on the motor development of infants with cerebral palsy (CP). The significantly greater improvements observed in the EI group's gross motor function, as measured by the GMFM-88, at both 6 and 12 months, underscore the critical role of EI in shaping the developmental trajectory of these children. This finding resonates with a burgeoning body of research that consistently points to the efficacy of EI in enhancing motor outcomes in children with CP. The remarkable improvements in motor function witnessed in this study are likely attributable to the multifaceted and tailored nature of the EI program, which judiciously integrated the principles of neurodevelopmental therapy (NDT) and sensory integration therapy. These therapeutic approaches, when applied in concert, provide a comprehensive framework for addressing the diverse motor challenges faced by infants with CP. NDT, a cornerstone of our EI program, focuses on facilitating normal movement patterns, promoting postural control, and ultimately enhancing functional skills. This approach recognizes that movement is not merely a series of isolated muscle contractions but rather a complex interplay of sensory input, motor planning, and biomechanical principles. By meticulously analyzing an infant's movement patterns, therapists can identify and address underlying impairments that hinder optimal motor performance. Infants with CP often develop compensatory movement patterns due to muscle weakness, spasticity, or impaired coordination. These compensatory patterns, while initially helpful, can become ingrained and ultimately hinder the development of more efficient and functional movements. NDT therapists work to inhibit these atypical patterns and facilitate more typical movements by providing carefully graded sensory input and manual guidance. This may involve gently guiding an infant's limbs through a desired movement pattern, providing weight-bearing experiences to strengthen weak muscles, and facilitating postural adjustments to improve balance and stability. Postural control is the foundation upon which all other motor skills are built. Infants with CP often struggle with maintaining postural stability due to muscle weakness, spasticity, and impaired sensory processing. NDT therapists prioritize the development of postural control by providing a variety of experiences that challenge the infant's balance and postural reactions. This may involve placing the infant in different positions, such as sitting, kneeling, or standing, and providing support as needed to encourage active postural adjustments. By strengthening core muscles, improving postural alignment, and enhancing sensory feedback, therapists can help infants develop a stable base of support for more advanced motor skills. The ultimate goal of NDT is to enhance functional skills, enabling infants with CP to participate more fully in their daily lives. This may involve improving their ability to reach and grasp objects, roll, crawl, sit, stand, walk, and interact with their environment. NDT therapists work closely with families to identify functional goals that are meaningful to the child and family, and then design interventions that promote the acquisition of these skills. This may involve practicing specific movements, adapting the environment to facilitate participation, and providing assistive devices as needed. NDT emphasizes the importance of active participation and engagement in the therapeutic process. By encouraging infants to explore their environment, interact with objects, and make choices, therapists can foster motor learning and promote the development of problem-solving skills. This active learning approach not only enhances motor skills but also fosters cognitive development, self-confidence, and motivation. Sensory integration therapy, another integral component of our EI program, addresses the often-overlooked sensory challenges faced by infants with CP. Children with CP frequently experience difficulties in processing sensory information, which can manifest as over-sensitivity or under-sensitivity to touch, movement, or sounds. These sensory processing difficulties can significantly impact motor planning, coordination, and adaptive responses to the environment. Sensory modulation refers to the ability to regulate and organize sensory input. Infants with CP may exhibit difficulties with sensory modulation, either over-responding or under-responding to sensory stimuli. Sensory integration therapy aims to help infants develop more appropriate responses to sensory input by providing a carefully calibrated sensory diet. This may involve activities that provide calming and organizing sensory input, such as deep pressure touch, rhythmic movement, or soft music, for infants who are over-responsive. For infants who are under-responsive, therapists may provide more intense and alerting sensory input, such as fast swinging, vibrating toys, or bright lights. Sensory discrimination refers to the ability to distinguish between different sensory stimuli. Infants with CP may have difficulty discriminating between different textures, shapes, sounds, or movements. Sensory integration therapy provides opportunities for infants to practice and refine their sensory discrimination skills through a variety of activities that involve exploring different sensory stimuli. This may involve sorting objects by texture, matching sounds, or identifying different body positions. Sensory-based motor planning refers to the ability to use sensory information to plan and execute movements. Infants with CP may struggle with sensory-based motor planning due to difficulties in processing sensory feedback and integrating it with motor commands. Sensory integration therapy provides opportunities for infants to practice and refine their sensory-based motor planning skills through activities that require them to use sensory information to guide their movements. This may involve navigating obstacle courses, building towers, or engaging in pretend play scenarios that require motor planning and problem-solving. Sensory integration therapy recognizes the fundamental interconnectedness of sensory processing and motor planning. By improving sensory processing, therapists can indirectly enhance motor planning and coordination. For instance, improved body awareness and spatial orientation can lead to more efficient and coordinated movements. Similarly, improved tactile discrimination can enhance fine motor skills and hand-eye coordination. The home-based nature of our EI program further amplifies its effectiveness. Infants are more likely to transfer newly acquired motor skills to their everyday routines and activities when they are learned in a familiar context. The home environment provides a natural and authentic setting for practicing and applying new motor skills. For instance, an infant who learns to pull to stand at a therapy table is more likely to generalize this skill to pulling to stand at furniture pieces throughout the home. The home environment offers a rich and varied landscape for motor learning. Everyday objects and activities can be seamlessly integrated into therapeutic interventions, making therapy more engaging and meaningful for the child. For instance, reaching for a favorite toy, crawling towards a caregiver, or climbing onto a sofa can all become opportunities for practicing and refining motor skills. The home environment also provides a natural source of motivation, as infants are inherently driven to explore and interact with their surroundings. The home-based approach fosters active involvement of parents or caregivers in the therapeutic process. By empowering families to participate in their child's therapy, we not only enhance the frequency and intensity of intervention but also create a more supportive and conducive environment for motor learning. Parents and caregivers become active partners in their child's development, reinforcing therapeutic techniques and integrating them into daily routines. This collaborative approach strengthens the parent-child bond and fosters a sense of shared responsibility for the child's progress. The sustained improvement in motor function observed in the EI group from 6 to 12 months highlights the enduring benefits of early intervention. This finding underscores the importance of providing ongoing support and intervention to children with CP to maximize their motor potential and prevent secondary complications. Early intervention is not merely a short-term fix but rather a long-term investment in a child's future. By intervening early and consistently, we can help children with CP build a strong foundation for motor development, which can have cascading positive effects on their overall development and quality of life. Motor skills are essential for exploring the environment, interacting with others, and learning new concepts. By improving motor skills, EI can pave the way for cognitive, social, and emotional development. Sustained intervention can help prevent secondary complications that often arise in children with CP, such as contractures, deformities, and pain. Contractures are the shortening of muscles or tendons, which can limit joint movement and cause deformities. Deformities can lead to pain, difficulty with mobility, and limitations in daily activities. By maintaining muscle flexibility, promoting joint range of motion, and encouraging active movement, therapists can help children with CP maintain their physical well-being and prevent the development of secondary impairments.[11-13]

Our study delves into the neural underpinnings of motor improvement in infants with CP by utilizing advanced neuroimaging techniques, specifically diffusion tensor imaging (DTI) and functional magnetic resonance imaging (fMRI). These powerful tools allow us to peer into the intricate workings of the brain and uncover the subtle yet significant changes in brain structure and function that accompany motor gains. DTI provides a unique window into the microstructural properties of white matter, the brain's intricate network of communication pathways. By tracking the movement of water molecules along axons, the brain's nerve fibers, DTI can reveal subtle alterations in white matter integrity, including changes in myelination, axonal density, and fiber organization. Our DTI findings highlight a key benefit of early intervention, increased fractional anisotropy (FA) in the corticospinal tract and corpus callosum of infants in the EI group at 12 months. FA is a measure of the directionality of water diffusion in white matter, reflecting the coherence and organization of axons. Higher FA values generally indicate greater white matter integrity, suggesting more efficient and reliable communication between brain regions. The corticospinal tract is a vital pathway for voluntary motor control, originating in the motor cortex and extending down to the spinal cord, where it relays signals to muscles throughout the body. Damage to this pathway, common in CP, can lead to muscle weakness, spasticity, and impaired coordination. The increased FA values observed in the corticospinal tracts of infants in the EI group suggest that early intervention promotes the development and maturation of this crucial pathway. This enhanced white matter integrity may facilitate more efficient transmission of neural signals from the brain to the muscles, contributing to improved motor control and coordination. The corpus callosum is the largest white matter structure in the brain, serving as a bridge between the two hemispheres. It plays a critical role in integrating information from both sides of the body and coordinating movements that involve both limbs. In infants with CP, damage to the corpus callosum can disrupt interhemispheric communication, leading to difficulties with bilateral coordination and motor planning. The increased FA values observed in the corpus callosum of infants in the EI group suggest that early intervention strengthens this interhemispheric connection, promoting more efficient communication and coordination between the two sides of the brain. These DTI findings provide compelling evidence that early intervention not only improves motor skills but also fosters the development and maturation of white matter pathways critical for motor control. This enhanced white matter integrity may lay the foundation for more efficient and coordinated movements, enabling infants with CP to explore their environment, interact with others, and achieve greater independence in daily activities. fMRI offers a dynamic view of brain function, capturing the intricate interplay between different brain regions. By detecting changes in blood flow associated with neural activity, fMRI can reveal which brain regions are engaged during specific tasks or even at rest. Our fMRI findings reveal another layer of neural plasticity induced by early intervention stronger functional connectivity between key motor-related brain regions in infants in the EI group at 12 months. Functional connectivity refers to the temporal correlation of activity between different brain regions, reflecting the degree of communication and coordination within a network. The primary motor cortex is the brain's command center for voluntary movement, sending signals down the corticospinal tract to initiate and control muscle contractions. The premotor cortex, located just in front of the primary motor cortex, plays a crucial role in planning and preparing for movement, selecting appropriate motor programs based on sensory input and goals. The enhanced functional connectivity observed between these two regions in infants in the EI group suggests that early intervention promotes more efficient communication and coordination between motor planning and execution centers. This may lead to smoother, more fluid movements and improved motor control. The supplementary motor area, located on the medial surface of the brain, is involved in higher-level motor planning, particularly for complex sequences of movements and internally generated actions. It plays a crucial role in coordinating bimanual movements, those involving both hands, and in selecting appropriate motor responses based on internal goals and intentions. The enhanced functional connectivity observed between the primary motor cortex and supplementary motor area in infants in the EI group suggests that early intervention promotes more efficient communication and coordination between motor execution and higher-level motor planning centers. This may lead to improved motor planning, sequencing, and execution of complex movements. These fMRI findings provide further evidence that early intervention not only strengthens individual motor pathways but also fosters the development of more efficient and integrated motor networks. This enhanced network organization may contribute to better motor planning, coordination, and execution of movements, enabling infants with CP to engage more fully in their environment and achieve greater motor milestones.[14-16]

Our correlation analysis revealed a compelling narrative of interconnectedness between brain plasticity and motor improvement in infants with CP who received early intervention. The significant positive associations between changes in GMFM-88 scores and all three neuroimaging measures – FA in the corticospinal tract, FA in the corpus callosum, and functional connectivity between the primary motor cortex and premotor cortex – underscore the profound interplay between brain and behavior. These findings provide further support for the notion that early intervention not only enhances motor skills but also induces beneficial changes in the brain, changes that are intricately linked to motor gains. Traditionally, the effectiveness of interventions for children with CP has been primarily assessed through behavioral measures, such as standardized motor assessments like the GMFM-88. While these measures provide valuable information about a child's functional abilities and progress, they offer limited insight into the underlying neural processes that drive motor performance. By incorporating neuroimaging measures into our analysis, we gain a more comprehensive understanding of how early intervention influences brain development and how these changes relate to motor outcomes. Neuroimaging provides a window into the intricate workings of the brain, allowing us to visualize and quantify changes in brain structure and function. In our study, DTI and fMRI revealed significant changes in white matter integrity and functional connectivity in infants who received early intervention. These changes, in turn, were strongly correlated with improvements in motor function, suggesting that early intervention not only enhances motor skills but also promotes beneficial changes in the brain that support motor learning and performance. The stronger correlations between changes in GMFM-88 scores and FA values, compared to the correlation with functional connectivity, highlight the critical role of white matter integrity in motor development. White matter, as the brain's communication network, provides the infrastructure for efficient and coordinated neural signaling. The integrity of white matter pathways, particularly those involved in motor control, is essential for transmitting signals from the brain to the muscles, enabling precise and coordinated movements. In infants with CP, damage to white matter can disrupt neural communication, leading to motor impairments such as muscle weakness, spasticity, and poor coordination. Early intervention, by promoting the development and maturation of white matter, can enhance the efficiency of neural signaling, contributing to improved motor skills. Our findings suggest that white matter integrity may be a particularly important factor in predicting motor improvements in infants with CP who receive early intervention. The correlation analysis also sheds light on individual differences in treatment response. While the overall trend indicates a positive association between brain changes and motor improvement, the strength of this association may vary across individuals. This suggests that some infants may experience greater benefits from EI in terms of both brain plasticity and motor gains, while others may show more modest improvements. Understanding these individual differences is crucial for tailoring interventions to meet the specific needs of each child. Future research may explore factors that contribute to individual differences in treatment response, such as the extent of brain injury, the timing and intensity of intervention, the child's genetic makeup, and environmental factors. By identifying these factors, we can develop more personalized interventions that maximize the potential for brain plasticity and motor improvement in each child. The findings of our correlation analysis have far-reaching implications for the field of neurorehabilitation. By demonstrating a clear link between brain plasticity and motor outcomes, our study reinforces the importance of targeting both brain and behavior in interventions for children with CP. This knowledge can guide the development of more targeted and effective interventions that aim not only to improve motor skills but also to promote brain plasticity. For instance, interventions that specifically target white matter development, such as those that incorporate intensive motor practice, sensory stimulation, and cognitive challenges, may lead to greater motor gains in infants with CP. Furthermore, neuroimaging techniques can be used to monitor brain changes in response to intervention, providing valuable feedback on the effectiveness of different therapeutic approaches. This can help clinicians tailor interventions to individual needs and optimize treatment outcomes.[17,18]

The findings of this study have far-reaching implications for clinical practice and future research in the field of pediatric rehabilitation. By providing compelling evidence for the efficacy of early intervention (EI) in promoting motor development and inducing beneficial changes in brain structure and function in infants with CP, our study underscores the critical importance of early identification and intervention to maximize the developmental potential of these children. Healthcare professionals, including pediatricians, neurologists, and developmental specialists, should be vigilant in identifying infants who may have or be at risk for CP. Early signs of CP may include delayed motor milestones, abnormal muscle tone, and persistent primitive reflexes. When CP is suspected, prompt referral to EI programs is crucial to initiate intervention as early as possible. The earlier the intervention, the greater the potential for harnessing the brain's natural plasticity and shaping the trajectory of motor development. EI services should be comprehensive and tailored to the unique needs of each child and family. A multidisciplinary team, including physical therapists, occupational therapists, speech-language pathologists, and early childhood educators, should collaborate to develop an individualized intervention plan that addresses the child's specific motor, cognitive, communication, and social-emotional needs. EI programs should incorporate evidence-based approaches, such as NDT and sensory integration therapy, which have been shown to be effective in promoting motor development and enhancing sensory processing in children with CP. These approaches should be implemented by qualified therapists who have received specialized training in these techniques. The home-based nature of intervention should be emphasized to facilitate generalization of skills and active involvement of families. By embedding therapeutic activities within the child's natural environment, we can promote the transfer of newly acquired skills to everyday routines and activities. Furthermore, involving families in the intervention process empowers them to become active participants in their child's development, fostering a sense of collaboration and shared responsibility. Regular monitoring and follow-up are essential to track the child's progress, adjust intervention strategies as needed, and address any emerging challenges. The multidisciplinary team should work closely with the family to assess the child's development, provide ongoing support, and ensure that the intervention plan remains aligned with the child's evolving needs.[19,20]

5. Conclusion

Our study underscores the profound impact of early intervention (EI) on infants with cerebral palsy (CP) in Surabaya, Indonesia. By significantly improving motor outcomes, EI not only enhances the children's developmental trajectory but also fosters neuroplasticity, leading to improved white matter integrity and functional connectivity in motor-related brain regions. These findings highlight the critical role of EI in shaping the future of these children and underscore the importance of prompt referral to EI programs upon CP diagnosis. The study also emphasizes the importance of comprehensive, individualized EI services tailored to each child and family. This includes a multidisciplinary team approach, incorporating evidence-based approaches like NDT and sensory integration therapy, implemented by qualified therapists. The home-based nature of intervention facilitates the generalization of skills and active family involvement, promoting the transfer of newly acquired skills to daily routines. In conclusion, our study provides compelling evidence supporting the efficacy of early intervention in promoting motor development and inducing beneficial changes in brain structure and function in infants with CP. By investing in EI, we can help these children build a strong foundation for their future, enabling them to reach their full potential and achieve greater independence.

6. References

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