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Tactile Stimulation and Active-Assisted Exercise on Motor Function and Functional Ability of Upper Extremity in Post-Stroke Patients

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ABSTRACT

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Keywords:

Active exercise; Functional recovery; Motor recovery; Somatosensory stimulation. Post-stroke sensorimotor disorders are the leading cause of long-term disability in adults. The purpose of this research was to analyze the combined effect of tactile stimulation and active-assisted exercise on upper-extremity motor function and functional activity in post-stroke patients at Physio Dahsyat Home Care. A Quasi-Experimental Design was used with purposive sampling. Thirty participants were divided into two groups: Group A, a combination of tactile stimulation and active assisted exercise; and Group B, electrical stimulation and PNF. The average scores of FMA-UE and CAHAI-8 in Group A were 16.33 to 60.13 and 14.80 to 52.73. In Group B, the average score was 13.40 to 48.07 and 13.40 to 44.87. Paired t-tests showed pvalues<0.001 for both Group A and Group B, indicating a significant effect in both groups. An independent test showed a significant. < 0.001, indicating a comparison of the impact on motor function and functional activity of the upper extremity. The highest average scores for motor function and functional activity in Group A were 60.13 and 52.73. A combination of tactile stimulation and active-assisted exercise was more effective, leading to increased muscle strength through motor unit activation; the more motor units involved, the greater the increase in muscle strength.



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INTRODUCTION

Stroke, as the leading cause of disability in adults, maintains its stability in the burden of noncommunicable diseases (NCDs) in high-income countries. On the other hand, in middle- and low-income countries, there has been an increase of nearly 50% in the number of stroke cases from the total burden of similar diseases. This trend change appears to be linked to population aging and increases in cardiovascular disease risk factors. Stroke is the second leading cause of death and disability worldwide. Stroke itself is not a single disease but can be caused by various risk factors, disease processes, and diverse mechanisms (Murphy & Werring, 2020). According to the World Stroke Organisation (in Martins, 2025), there are approximately 93.8 million people worldwide living as stroke survivors, with the majority (approximately 87% of deaths and 89%) of DALYs) occurring in low- and middle-income countries. Since 1990, the incidence of stroke has increased by approximately 70%, prevalence has increased by approximately 86%, and mortality has increased by approximately 44% globally, indicating a growing burden of stroke. Meanwhile, in Indonesia itself, according to the results of the 2023 Indonesian Health Survey (SKI), the prevalence of stroke is 8.3% or 638,178 people, particularly in East Java, at 9% or 98,378 people, with a disability rate of 21.3%. A preliminary study conducted at Physio Dahsyat home care noted that since 2024, there has been an increase of approximately 15 stroke patients each month, with a total of 215 patients in that year.

Post-stroke neuromotor disorders are the primary cause of long-term disability in adults.

Flaccid paralysis is the most severe motor disorder following a stroke, characterized by weakness and reduced muscle tone. One common complication of stroke is weakness in the upper extremity, which affects up to 80% of stroke survivors and impairs their ability to perform daily activities. The complexity of upper extremity movements during normal daily activities and the various phenotypes of upper extremity movements after stroke are primarily explained by kinematics and muscle activation (Faccioruso et al., 2024). The flaccid phase can last for months or even years in some individuals who have experienced a stroke. Prolonged flaccidity impairs independence and accelerates disability.

Meanwhile, spasticity commonly contributes to soft-tissue contraction by excessively engaging shortened muscles, driven by heightened stretch reflexes. This constricted state is referred to as a "synergy," characterized by a pattern of tightness. In clinical practice, characteristic flexion synergies in the upper extremities after stroke include scapular elevation and internal rotation, glenohumeral joint abduction and external rotation, elbow flexion, forearm supination or pronation, and wrist and finger flexion (Liu et al., 2021).

Recovery after a stroke is enhanced by neuroplasticity, which is the reorganisation of neural networks that facilitates the recovery of motor skills. Research on motor learning in humans and other animals shows that motor rehabilitation can promote post-stroke somatosensory recovery. Brain areas processing somatosensory information, including the posterior parietal cortex, are closely associated with motor planning areas in the frontal lobe. This sensorimotor network undergoes functional changes and sustained connectivity after motor learning (Borstad et al., 2022). Lack of physical activity is associated with an increased risk of recurrent stroke. Physical therapists are well-positioned to encourage physical activity. The lack of attention to rehabilitation following a stroke has led most rehabilitation service providers to focus on compensatory strategies for enhancing function rather than restoring motor control. Increased activity in cortical and subcortical motor areas is the primary mechanism for motor function recovery during neurorehabilitation. Various interventions can be used for post-stroke recovery, such as bilateral training, repetitive task training, constraint-induced movement therapy, electrical stimulation (ES), and exercise. Among these interventions, physical exercise is critical as it helps patients return to daily activities by restoring impaired motor function and improving physical function (Lee et al., 2022). Exercise is a therapeutic method that can activate these areas and stimulate an increase in the cascade of trophic and growth factors, ultimately facilitating neuroplasticity and motor recovery.

Tactile stimulation exercises, which involve processing somatosensory information, including the posterior parietal cortex, are closely associated with the frontal motor planning area of the lobe. This sensorimotor network undergoes long-lasting functional changes and alterations in connectivity following motor learning (Borstad et al., 2022). Previous research indicates that performing active-assisted exercises can enhance muscle strength by stimulating motor units. By engaging more motor units, muscle strength can be increased. Providing active-assisted exercise can increase muscle strength by activating motor units; the more motor units involved, the greater the increase in strength. The combination of tactile stimulation and active-assisted exercise has not received sufficient attention, despite the expanding body of research on post-stroke rehabilitation, especially in upper-extremity motor recovery. The majority of stroke survivors have upper extremity impairment, which significantly contributes to long-term disability. Therefore, it is critical to find accessible and effective therapeutic approaches. Tactile stimulation can enhance somatosensory input and facilitate sensorimotor integration, whereas activeassisted exercise can enhance early motor engagement and support neuroplastic processes. However, empirical research assessing the synergistic effect of these two therapies is currently lacking. To close current gaps in rehabilitation techniques and develop more thorough, efficient methods to enhance motor function and functional activity, it is crucial to examine the use of tactile stimulation and active-assisted exercise.

METHOD

This study constitutes a quantitative research employing a quasi-experimental method with a non-equivalent control group design. The research was conducted at Physio Dahsyat Home Care

from January 2025 to February 2025. The sampling technique utilized was purposive sampling. The study population comprised 40 patients, of whom 30 met the inclusion and exclusion criteria. The inclusion criteria comprised patients diagnosed with stroke for ≥ 1 week and ≤ 6 months; aged ≥ 20 years to ≤ 75 years; with muscle weakness and unable to move their joints fully with a minimum MRC score of 2 and a maximum of 3; and an Ashworth scale ≤ 2 . Exclusion criteria included patients with comorbidities such as dementia, cognitive impairment, or Parkinson's disease; fractures or dislocations in the area affected by hemiparesis; visual or hearing impairment; GCS score ≤ 12 ; and hemiparesis on both sides of the body. This study was divided into two groups: group A, the experiment group, with a combination of tactile stimulation and active-assisted exercise, and group B, the control group, with electrical stimulation and PNF. The research was conducted over 4 weeks, with 3 sessions per week.

Table 1. Active-assisted exercise protocol

Region	Movement	How to apply		
Shoulder	Flexion-Extension	The physiotherapist stabilizes the elbow and instructs the patient to perform shoulder flexion and extension with the physiotherapist's assistance.		
Elbow	Flexion-Extension	The physiotherapist stabilizes the elbow and instructs the patient to perform elbow flexion and extension (similar to washing hair) with the physiotherapist's assistance.		
Wrist	Dorsiflexion- Palmarflexion	The physiotherapist stabilizes the wrist and instructs the patient to perform dorsiflexion-plantarflexion of the wrist with the physiotherapist's assistance.		
Finger	Flexion-Extension	The physiotherapist stabilizes the proximal finger area and instructs the patient to perform finger flexion and extension with the physiotherapist's assistance.		

In each rehabilitation session facilitated by a physiotherapist, the session is divided into two phases. The first phase was tactile stimulation training, followed by the second phase on active-assisted exercise. Before starting the interventions, stretching was provided in each region of the upper extremity. Tactile stimulation is aimed at enhancing hand sensibility, enabling the patient to discern textures, consistencies, sizes, and weights of various objects. During the first 5 minutes, specific movements were performed to reduce muscle tone in the patient's hand and leg. This involved applying pressure at the metacarpophalangeal joints and performing passive mobilization of the thenar and hypothenar muscle groups, as well as the interossei.

Additionally, tactile stimulation was administered to the prepared hand. Tactile stimulation using a physiotherapist's hand to stimulate the hand at the external edge, internal edge, thenar eminence, hypothenar eminence, flexion line, interdigital space, and fingertips. The active-assisted exercise phase was carried out in 4 sets (8 repetitions) and aimed to engage more motor units to increase muscle strength. This involved upper-extremity movement, which was considered to inhibit the synergistic pattern (see Table 1). This combination exercise was performed for 45 minutes per session, 3 times a week for 4 weeks.

The research instruments employed to assess upper extremity motor function and functional ability were the Fugl-Meyer Assessment Upper Extremity (FMA-UE) and the Chedoke Arm and Hand Activity Inventory-8 (CAHAI-8). Instruments were given directly to respondents before and after the interventions. The FMA-UE scale has 33 items and is scored on a 3-point scale: 0 means unable to do; 1 means able to do partially; 2 means able to do completely. The CAHAI-8 scale has 8 questions. Scoring is done on a 7-point scale similar to the FIM. For each item, the score can range from 1 (i.e., the affected limb performs less than 25% of the task) to 7 (i.e., the affected limb completes all required components). Data analysis was performed using a statistical application, which included normality tests to assess data normality, paired t-tests to determine the effect of Group A and Group B, and independent t-tests to compare the groups. This study has received ethical approval from Universitas **STRADA** Indonesia, clearance 0023468/EC/KEPK/I/01/2025.

RESULTS

Table 2. Demographic characteristics of group A

Data characteristic	Group A				
Data Characteristic	f	%			
Age					
17 – 25 years	1	7			
26 – 35 years	3	20			
36 – 45 years	1	7			
46 – 55 years	8	53			
56 – 65 years	1	7			
> 65 years	1	7			
Gender					
Male	10	67			
Female	5	33			
Stroke classification					
Ischemic	13	87			
Hemorrhagic	2	13			
Lesion side	Lesion side				
Sinistra	7	47			
Dextra	8	53			
Duration of stroke					
≤4 weeks	2	13			
>4 weeks	13	87			

Table 2 shows the 46-55 age (8 p) group obtained the highest score, followed by male gender (10 p), is chaemic stroke classification (13 p), right-sided lesions (8 p), and stroke duration >4 weeks (13 p).

Table 3. Demographic characteristics of group B

Data characteristic	Group B			
Data characteristic	f	%		
Age				
17 – 25 years	0	0		
26 – 35 years	1	7		
36 – 45 years	2	13		
46 – 55 years	2	13		
56 – 65 years	8	53		
> 65 years	2	13		
Gender				
Male	8	53		
Female	7	47		
Stroke classification				
Ischemic	14	93		
Hemorrhagic	1	7		
Lesion side				
Sinistra	5	33		
Dextra	10	67		
Duration of stroke				
≤4 weeks	3	20		
>4 weeks	12	80		

Table 3 shows the 56-65 age (8 p) group obtained the highest score, followed by male gender (8 p), ischaemic stroke classification (14 p), right-sided lesions (10 p), and stroke duration >4 weeks (12 p).

Table 4. Score before intervention

	Variable	Mean + SD
Group A	Motor function	16.33 + 13.61
	Functional activity	14.80 + 6.721
Group B	Motor function	13.40 + 9.568
	Functional activity	13.40 + 4.579

Table 4 shows the average motor function and functional activity scores for the upper extremity before intervention in the experimental group were 16.33 and 14.80, respectively. In the control group, the average upper-extremity motor function and functional activity scores before intervention were 13.40 and 13.40, respectively.

Table 5. Score after intervention

	Variable	Mean + SD
Group A	Motor function	60.13 + 5.208
	Functional activity	52.73 + 2.549
Group B	Motor function	48.07 + 6.974
	Functional activity	44.87 + 4.307

Table 5 shows the average motor function and functional activity scores for the upper extremity in the experimental group after intervention were 60.13 and 52.73, respectively. In the control group, the average upper-extremity motor function and functional activity scores before intervention were 48.07 and 44.87, respectively.

Table 6. Normality test

	Variable		Sig.
Group A	Motor function	Pre-test	0.058
		Post-test	0.154
	Functional activity	Pre-test	0.059
		Post-test	0.057
Group B	Motor function	Pre-test	0.170
		Post-test	0.072
	Functional activity	Pre-test	0.068
		Post-test	0.054

The results of the Shapiro-Wilk normality test in Table 6, all groups in the pre-test and post-test had a Sig. Value> 0.05. Therefore, the data are normally distributed.

Table 7. Effect of group A and group B on motor function and functional activity

	Variable		Mean ± SD	Sig. 2-tailed
Group A	Motor function	Pre-test	16.33 ± 13.610	< 0.001
		Post-test	60.13 ± 5.208	< 0.001
	Functional activity	Pre-test	14.80 ± 6.721	< 0.001
		Post-test	52.73 ± 2.549	< 0.001
Group B	Motor function	Pre-test	13.40 ± 9.568	< 0.001
		Post-test	48.07 ± 6.974	< 0.001
	Functional activity	Pre-test	13.40 ± 4.579	< 0.001
		Post-test	44.87 ± 4.307	< 0.001

The paired t-test results for the experimental group in Table 7, the p-value was 0.000, which is <0.05. There is an effect of the combination of tactile stimulation and active-assisted exercise on upper-extremity motor function and functional activity in post-stroke patients. Meanwhile, in the control group, the p-value (0.000) was <0.05. It can be concluded that the control group has an effect on motor function and upper extremity functional activity in post-stroke patients.

Table 8. Comparison of the effect of group A and group B on motor function and functional activity

		Mean ± SD	Sig. 2-tailed
Motor function	Group A	60.13 ± 5.208	< 0.001
	Group B	48.87 ± 8.017	< 0.001
Functional activity	Group A	52.73 ± 2.549	< 0.001
	Group B	44.87 ± 4.307	< 0.001

The independent t-test for the experimental group in Table 8, the p-value was 0.000, which is < 0.05. Meanwhile, also in Table 8, the highest average scores for motor function and functional activity of the upper extremity in the experimental group were 60.13 and 52.73, respectively. Therefore, it can be concluded that the combination of active-assisted exercise and tactile stimulation has a greater effect on upper extremity motor function and functional activity than the control group in post-stroke patients.

DISCUSSION

Identification of motor function and functional activity of the upper extremity before and after in group A

Results indicating that the combination of tactile stimulation and active-assisted exercise affected motor function and upper-extremity functional activity in post-stroke patients. This aligns with the study by Chen et al. (2025) on tactile stimulation, which found that tactile feedback can modulate brain activity in areas related to motor learning and sensorimotor integration, providing evidence of its potential as a valuable intervention in the rehabilitation of post-stroke patients. Another study by Zandvliet et al. (2020) also states that in the early stages after a stroke, spontaneous neurobiological recovery drives somatosensory recovery. With appropriate treatment involving activation and facilitation, this can promote recovery in stroke patients.

Movement increases afferent input from muscles, joint receptors, and skin mechanoreceptors. Additionally, upper extremity motor rehabilitation typically involves object manipulation that directly stimulates skin receptors. Through parallel pathways, somatosensory information from touch and proprioception is processed in extensive cortical networks. The bidirectional interaction between somatosensation and movement supports sensorimotor learning, which is associated with changes in the motor and somatosensory systems (Borstad et al., 2022). Brain areas processing somatosensory information, such as the posterior parietal cortex, have close connections with motor planning areas in the frontal lobe. This sensorimotor network undergoes lasting changes in function and connectivity following motor learning. Although the exact mechanisms are not fully understood, one possibility is positive neural adaptation due to increased somatosensory input during movement (Borstad et al., 2022).

Research by Lee et al. (2022) on active-assisted exercise suggests that active motor rehabilitation is necessary rather than unrestricted rest, even in the early stages. Additionally, research by Zandvliet et al. (2020) suggests that somatosensory input through active-assisted exercise can promote experience-dependent plasticity, which underpins neural circuit remodeling. Therefore, it can assist in motor rehabilitation programs following a stroke. This exercise still requires active patient participation, thus necessitating good cognition and high motivation. Optimal cognition enables patients to follow therapists' instructions effectively, promoting neuroplasticity to activate remaining brain areas to compensate for functions lost due to stroke. This process supports the brain's adaptation in optimizing movement (Syah et al., 2020). The neural mechanisms involved in post-stroke somatosensory recovery include increased functional connectivity in the parietal operculum, thalamic reorganization, enhanced processing of afferent input, and cortical reorganization (Van de Winckel et al., 2020). Post-stroke motor recovery is closely related to the motor learning process, where the premotor cortex (PM), as part of the mirror neuron system, plays a role in learning through observation and motor control (Mihara et al., 2021).

The findings show that the combination of tactile stimulation and active-assisted exercise

significantly improves post-stroke patients' motor function and upper extremity functional activity. This implies that physical movement and tactile input can improve sensorimotor integration and promote healing by altering neuroplasticity. Increased sensory input from muscles, joints, and skin during motor activity improves somatosensory processing and encourages adaptive changes in the motor and sensory systems. Patients can engage in motor learning and stimulate brain circuits that compensate for lost functions through active-assisted exercise, which promotes active engagement while offering essential help. Effective learning and functional recovery are made possible by further optimising this process through adequate cognitive function and motivation. The combined intervention improves cortical remodelling and afferent input, which improves upper extremity motor control and functional performance. Overall, these results demonstrate that combining tactile stimulation with active-assisted exercise can be a practical post-stroke rehabilitation approach that supports somatosensory and motor recovery through experience-dependent neuroplasticity.

Identification of motor function and functional activity of the upper extremity before and after in group B

Based on the paired t-test in Table 7, the p-value was <0.001, indicating that the electrical stimulation intervention and the PNF control group both affected upper extremity motor function and functional activity in post-stroke patients. This aligns with the study conducted by Shahid et al. (2023, which states that electrical stimulation is an effective intervention for improving sensory function. Electrical stimulation enhances motor function. Electrical stimulation has effects in strengthening muscles, reducing spasticity, enhancing stimulation of the corticospinal nerve pathways, and improving neuroplasticity (Kristensen et al., 2022). Electrical stimulation triggers action potentials in motor nerves, activating motor units and producing effects such as strengthening the stimulated muscles, improving voluntary motor control, and reducing spasticity. Electrical stimulation can activate disrupted nerve pathways (Beijora et al., 2023).

Similarly, research by The et al. (2020) indicates that administering PNF exercise therapy can improve functional activity in post-stroke patients. This method stimulates the proprioceptive organs in muscles and tendons to improve muscle function, encourage postural reflex exploration, and prioritise muscle contraction to improve strength, flexibility, balance, and coordination (Nguyen et al., 2022). PNF is one of the most effective physical interventions for decreasing muscle spasticity and improving lower-limb function. Due to its effects on pain relief, range of motion, muscle strength and endurance, coordination, and improved proximal stability and functional progress, this method has been widely used in early rehabilitation during the acute or subacute phase to facilitate neuromuscular education and improve motor function in stroke patients. PNF operates on the principle that repeated commands, traction, approach, audiovisual cues, and stretch reflexes facilitate the transmission of impulses along the reflex arc to elicit sensory-motor responses. Electrical stimulation is designed to provide real-time feedback on patient performance, thereby enhancing motor and cognitive engagement during task execution. This is then reinforced through PNF-based exercise therapy. As a result, motor function improves, and more meaningful muscle contractions occur, making functional activities easier to achieve. The findings show that PNF training and electrical stimulation both significantly enhance upperextremity motor function and functional activity in stroke survivors. Electrical stimulation improves voluntary motor control and repairs damaged neural pathways by increasing muscle strength, decreasing stiffness, activating motor nerves, and fostering neuroplasticity. In the meantime, PNF training supports functional recovery by facilitating proprioceptive stimulation, encouraging postural reflexes, and improving muscle strength, flexibility, coordination, and balance. All things considered, both therapies successfully target motor and sensory systems, making them practical tactics in post-stroke rehabilitation to maximise upper extremity function

and everyday activity performance.

Identification of differences in the effects of motor function and functional activity of the upper extremity between group A and group B

Results indicating a significant difference between Group A and Group B regarding motor function and upper extremity functional activity in post-stroke patients, with Group A showing a more effective result. A study by Karaca & Kılınç (2024) found that combining sensory exercises with motor-focused exercise therapy is more effective at enhancing motor function and functional activity in post-stroke patients. This aligns with research conducted by Kitai et al. (2021, which found that motor rehabilitation with tactile stimulation feedback has the potential to be an effective intervention tailored to the specific impairments and needs of patients with somatosensory disorders.

Tactile stimulation addresses challenges ranging from hypersensitivity to sensory deficits by providing sensory stimulation that can be adjusted based on the patient's sensory profile. Tactile stimulation is designed to provide real-time information about the patient's performance, thereby enhancing motor and cognitive engagement during task execution (Chen et al., 2025). Patients' perceptions of tactile stimulation—such as haptic, visual, and auditory feedback—play a crucial role in its effectiveness by influencing task engagement and performance. The intensity of tactile stimulation is adjusted according to the patient's recovery stage, with thresholds set to align with their specific conditions and support motor and cognitive engagement (Kwon et al., 2020). Tactile stimulation activates proprioceptors in the skin, joints, and muscle spindles, which then send impulses to anterior motoneurons, causing brief contractions. These stimuli are transmitted via afferent nerves to the central nervous system (CNS), activating facilitation and inhibition mechanisms in the cortex. Increased afferent input can enhance tactile sensations following motor rehabilitation. In stroke patients, exercise increases afferent input from skin, muscle, and joint receptors, contributing to somatosensory cortex remodeling throughout life (Borstad et al., 2022). Repeated administration of tactile stimulation provides information to supraspinal mechanisms, resulting in integrated movement patterns that become functional movement sequences repeatedly.

Active-assisted exercise is a therapeutic exercise aimed at maintaining or improving natural joint movement to enhance motor function, thereby increasing muscle mass and tone. The administration of active-assisted exercise also stimulates motor function, as the greater the number of motor units involved, the greater the increase in muscle strength (Pratiwi, 2023). The mechanism underlying the administration of active-assisted exercises involves reactivation of pre-existing nerve connections, development of new connections, and axonal regeneration. The physiological effects of active-assisted exercises can stimulate neuromuscular and muscular chemical compounds, thereby increasing their activity. Stimulation through neuromuscular pathways enhances activation of extremity muscle nerve fibers, particularly parasympathetic nerves, which stimulate acetylcholine production and trigger contractions.

Meanwhile, the mechanism via muscular pathways, especially in smooth extremity muscles, enhances mitochondrial metabolism to produce ATP used by extremity muscles for contractions and to increase smooth muscle tone (Merdiyanti et al., 2021). By repeatedly administering active-assisted exercise, the likelihood of plasticity increases. This is because neurological dysfunction following stroke requires brain reorganization as a motor recovery strategy (Kitai et al., 2021).

The findings show that post-stroke patients' upper extremity motor function and functional activity differ significantly between Group A and Group B, with Group A showing more improvement. Because tactile stimulation provides flexible sensory input that improves motor and cognitive engagement, engages proprioceptors, and supports integrated movement patterns, it is more effective when combined with active-assisted exercise. Active-assisted exercise supports the reorganisation of brain networks and fosters neuroplasticity by increasing muscle strength, joint mobility, and neuromuscular activation. When combined, these therapies enhance functional performance, maximise motor recovery, and improve long-term rehabilitation results for stroke survivors.

Limitations of the study

Several limitations of this study should be considered. First, the results may not be as broadly applicable as they may be due to the limited sample size. Second, the study's brief duration prevented observation of the intervention's long-term consequences. Third, a quasi-experimental design, inherently non-randomized and prone to selection bias, was used in the study. To improve the evidence, more studies with larger samples, longer follow-up times, and randomised controlled designs are advised.

CONCLUSION

This study demonstrates that the combination of tactile stimulation and active-assisted exercise is more effective than electrical stimulation with PNF in improving upper extremity motor function and functional ability in post-stroke patients at Physio Dahsyat Home Care. In addition, this study has several limitations, including a small sample size, a short intervention duration, and a non-randomized study design. These findings suggest that this combination may be a practical rehabilitation approach for optimizing motor recovery and upper extremity functional performance in post-stroke patients. However, further research with a larger sample size is needed to confirm these results and to extend the study duration. In summary, the combination of tactile stimulation and active-assisted exercise is more effective than either alone in improving upper-extremity motor function and functional ability in post-stroke patients.

AUTHOR'S DECLARATION

Authors' contributions and responsibilities

FYE: Prepared and writing manuscript; **PDK:** Analyzed data and reporting evaluations; **AW:** Make conclusions and editing; **SFNL, NAA:** review, editing, finishing manuscript.

Availability of data and materials

All data are available from the authors.

Competing interests

The authors declare no competing interests.

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