

Effect of 12-Week Pilates Exercises on Reaction Time of Male Patients with Parkinson's disease

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Abstract

Introduction: Parkinson's disease is common in old age, with many motor and non-motor complications. The purpose of the extant study was to compare the effects of Pilates and Tai Chi exercises on the reaction time of male patients with Parkinson's disease.

Method: The present study was conducted based on a field study through pretest and posttest of two training groups and one control group. The statistical population comprised 106 men suffering from Parkinson's. The sample size was calculated using a purposive and convenient sampling method; 45 subjects (with an age average of 64.72±7.29) were chosen and then assigned to two Tai Chi and Pilates exercise groups and one control group. The data were collected through scales, chronometers, Kurtzke Expanded Disability Status Scale (EDSS), and Physical Activity Readiness Questionnaire (PAR-Q). Reaction time tests were performed for all three groups. Training groups did exercises in three one-hour sessions per week (for 12 weeks). Data analysis was done through SPSS-21 software.

Results: Findings indicated no difference between the effects of Pilates and Tai Chi exercises on the simple reaction time (SRT) (P>0.05). The main effect of stage and the interactive inter-stage effect were significant in the SRT group. This result showed a significant difference between the three groups' performance in SRT. In the posttest stage, the difference between the two training groups was more than the control group, and the Pilates group obtained the lowest mean value (540.66) among the three groups. Moreover, there was a significant difference between the effects of Pilates and Tai Chi exercises on the selective reaction time. Three studied groups performed differently in selective reaction time (P<0.05). There was a low difference between groups within the pretest stage, and the Pilates group indicated the shortest selective reaction time (958.4). However, the difference between the two training groups was more than the control group within the posttest stage, and the Pilates group obtained the lowest mean value (871.60).

Conclusion: According to the results, both traditional Tai Chi and Pilates exercise positively affected the improvement of selective reaction time. Hence, it is suggested to use the mentioned exercises to improve the performance of patients who have Parkinson's disease.

Keywords: Parkinson's disease, Tai Chi Exercise, Pilates, Reaction Time

Introduction:

Parkinson's disease (PD) is the second most common neurodegenerative disease and one of the general health dilemmas (Cai et al., 2018). PD is caused by insufficient dopamine production, which damages motor skills and voice (Devarajan & Ravi, 2019; Olivares et al., 2020). Loss of dopamine causes the movement disorder in neurons' hypokinetic movement disorder (Pahuja & Nagabhushan, 2018). Now, more than 10 million people suffer from PD worldwide (Ahouz & Golabpour, 2020). Aging is one of the factors causing an increase in the number of people suffering from PD (Hariharan, Polat, Sindhu, 2014). The symptoms of Parkinson's disease include tremor, slow movement, rigidity in muscles, impaired posture and balance, writing and speech changes (Marar et al., 2018). Reaction time (RT) is another motor characteristic that is possibly lost in patients with PD.

RT indicates decision-making speed and its efficiency. RT is defined as the time between unexpected stimulus presentation and response onset. RT is an important index indicating the main part of movements. In many rapid movements, one's success depends on the time they spend identifying the situation or stimulus movements, deciding how to react, and initiating a suitable response. RT is a significant factor in the daily movements of PD

patients and other people with motor disabilities, especially when they face external turmoil. Many studies have found the important role of physical activity level in determining RT. Spirduso carried out an interesting study to compare RTs in four groups of active and sedentary young and older men. Spirduso found that active older men and sedentary young men had similar RT, while there was a considerable difference between RTs of active and sedentary older men (Gallahoo & Ozmon, 2005). Physical activity improves metabolism, respiration, blood circulation, digestion, and the function of external secretory glands. The increased blood circulation in the central nervous system (CNS) is necessary for the lifespan of brain cells and information processing efficiency.

Moreover, physical activity improves the function of some cerebral peduncles. These factors have a positive effect on central areas of RT. The increased blood circulation in the lower extremities produces sufficient temperature for rapid conduction of nerve impulses to muscles affecting the more peripheral parts of RT. Spirduso explains that lack of physical activity may cause CNS dysfunction due to the increased effects, blood pressures, and higher pigment density (Gallahoo & Ozmon, 2005).

Advanced studies indicate that timely impressive exercises protect the defective nervous system, moderate PD development, improve motor function, reduce behavioral impairments, and postpone the loss of dopamine in the brain (Zeynalzadeh & Nazari Moghadam, 2020). On the other hand, the known principles of neuroplasticity have indicated the lasting effects of repetitive, informed, and purposeful, functional exercises on CNS. Some components, such as intensity, specificity, rigidity, and complexity of exercises, are important for neuroplasticity induction (Fox et al., 2012). The CNS changes while reacting to a specific physical activity accelerate the learning process and skill acquisition. Many studies have investigated the effect of exercises therapy on patients suffering from PD. In general, relevant findings have proved the vital role of exercises and timely rehabilitation in treating patients who live with PD (Zeynalzadeh & Nazari Moghadam, 2020).

Many studies have shown the positive effect of exercises on PD patients' motor symptoms, including motor function, daily activities, balance, and flexibility (Rosenthal & Dorsey, 2013). Through their positive effects on dopamine level, exercise and physical activity improve the function of PD patients, muscular nervous system's function, anatomical adaptations, breaking the negative cycle of disease, aging, and immobility. However, exercise reduces depression and improves physical activity, health-related quality of life, balance, gait speed among patients with PD (Johnson, 2013).

Pilates exercises have been recently introduced as new physical activity techniques (Seghatolselami et al., 2018). Pilates training includes focus and attention on the muscle and performing exercises. Over time, a person's mind understands the body better, making the mind more capable and balanced by repeating exercises. These exercises are highly suitable for mind-body awareness training and controlling balance positions based on the high-level muscular-nervous needs (Cherie et al., 2012). Pilates improves flexibility and mental relaxation, increases muscle strength, and keeps control of the spine and balance (Babavigit, 2009). Joseph Pilates believed that all body muscles, particularly the deep muscles that are motor drivers, must be strengthened and flexible in power and traction. When doing Pilates exercises, trainees take control of all muscles then a natural harmony occurs gradually by repeating exercises (Fathi, 2011). Many studies have shown the effect of Pilates' exercises on RT and other motor characteristics (Cherie et al., 2012; Rahmani et al., 2015).

Tai Chi training includes mind-body exercises with a moderate intensity that pave the way for more mental activities and improved cardiorespiratory and digestion (Nery et al., 2015). Tai Chi Chuan (TCC) has origins in ancient Chinese martial arts with different styles, including Chen, Yang, Wu-Hao that are different in terms of forms, so that some have 18 forms while others have 100 forms. TCC techniques include relaxation, deep breathing, mindfulness, meditation, and gentle and harmonious stretching movements (Jiménez-Martín et al., 2018). TCC is more recommended for older people among Tai Chi styles since this style presents monotone

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movements with moderate intensity (Port et al., 2018). TCC first brings body balance then moderates the inner energy, mind, breathing, affections, and soul, leading to improved health (Janelsins et al., 2011). TCC exercises include some slow and steady movements in different body parts with relaxed, controlled movements, deep breathing, and correct posture with mindfulness and awareness. These fluid and slow movements strengthen the body and mind as a coherent and organized unit leading to calmness, longer life, and health (Huang & Liu, 2015). This inexpensive sport does not require any specific equipment, so all motor limitations or wheelchairdependent people can do TCC exercises (Stephanie et al., 2009). Marandi et al. (2013) found that one Tai Chi exercise course could improve flexibility, balance, depressive symptoms, and sleep quality of older adults living in the nursing home. Norouzian et al. (2017) reported that six weeks of Ta Chi training improved quality of life, psychological health, physical functioning, and dynamic balance. Tai Chi exercises improve quality of life and increase independence and balance level. Few studies have been conducted on this exercise, and sufficient attempts have not been made to train specific patients TCC exercises (Li et al., 2006). Therefore, the present study can be an effective step to introduce this new exercise in Iran. On the other hand, there was no Iranian study on the effect of Pilates and Tai Chi exercises and their comparative impacts on rehabilitation of motor functions among male patients with PD. Therefore, the extant study aimed to compare the effects of Pilates and Ta Chi exercises on RT of male patients with PD.

Method

The present field study was conducted as pretest-posttest quasi-experimental research, including two training groups and one control group. The statistical population comprised 166 59-75-years older men with PD diagnosed by a neurologist. All subjects were members of Urmia Parkinson's Foundation associated with the Welfare Organization. The research program, type, intensity, duration, frequency, and implementation method were explained to patients. In the next step, participants filled out the PAR-Q questionnaire and signed the consent letter. According to Shailja Pandya et al. (2017), inclusion criteria were as follows: PD diagnosed by a neurologist, lack of cardiovascular, epilepsy, metabolic, psychological, and orthopedic (e.g., knee pain) diseases, and desire to participate in research. Participants who did not attend at least two-thirds of training sessions or experienced Parkinson's relapse were excluded. The individuals who desired to participate in the research referred to PD Foundation in Qom County, Iran. After the volunteers filled out medical forms and measured their weights and heights, they declared their tendency for involvement in the project by considering some points about the effectiveness of exercise in preventing diseases, dressing preparation, and daily diet explained by the researcher and physician. All participants took RT tests. According to pretest scores, participants were divided into three homogenous (two training groups and one control group). The Control group did not exercise and lived their normal life after the initial test, and the RT test was repeated after 12 weeks.

Experimental (or training) groups received a 12-week schedule of Pilates and Tai Chi exercises in three one-hour (8-9 am) sessions per week. RT test was repeated after 12 weeks and doing daily tasks. All of the tests and exercises were done in the Sports Complex of Qom University. Each session of the Pilates training program comprised warmup (5 minutes), main movements of stretch, resistance, neuromuscular harmony, balance, and final 10-minute stretching for cooldown (Shanazari et al., 2012; Anbari et al., 2011). Tai Chi exercises were done based on the Wolf Training Program (2017). Yang TCC style was done three times (45-60 min) per week (Khesali et al., 2016). Post-test was performed after 24 TCC training sessions.

Data collecting instruments were digital scales (AND-EK3000I, Japan) to measure weight and height of subjects, chronometer (Q & Q, Japan) to record time, strip meter to measure distances, 50-cm ruler, Kurtzke Expanded

Disability Status Scale (EDSS) to assess physical disability, Physical Activity Readiness Questionnaire (PAR-Q), RT assessment software and device.

Kurtzke Expanded Disability Status Scale (EDSS): physical disability of participants was measured by EDSS, which was developed by Kurtzke (1993) to assess different states and functions of CNS, including functional systems of pyramidal, cerebellar, brainstem, sensory, bowel, and bladder, visual, and cerebral. EDSS gives a score between 0 and 10 to each PD patient regarding the injury level of CNS. The severer the injury, the higher the score will be. Accordingly, score 1 represents the lowest harm while 10 indicates death. This scale has been normalized in Iran. It should be noted that Fathi-Rezaie confirmed the reliability of this scale. Moreover, Shanazari et al. (2012) approved the validity and reliability of EDSS. In the extant study, the reliability of EDSS equaled 0.83. It is worth noting that this test must be done by a neurologist (Soltani et al., 2009).

Physical Activity Readiness Questionnaire (PAR-Q): PAR-Q evaluated the physical status of older adults with PD who wanted to participate in exercises (Thomas et al., 1993) by asking seven yes/no questions. The validity and reliability of the questionnaire have been confirmed in many studies. PAR-Q was also validated by Anbari et al. (2011). The present study reported reliability of 0.89 for this questionnaire.

Reaction Time Test (RTT): Timed Up and Go Test (TUG), 10-m walk test (10MWT), Stair Ascend/Descend Test, and 10-m walk test (6MWT) were used to test reaction time (Hider, 2011).

Descriptive analysis was done using mean and standard deviation. The repeated measures ANOVA and Tukey's post hoc test were employed for inferential analysis of data. Data analysis was done through SPSS-21 software.

Findings

Table 1 reports the participants' frequency, mean, and standard deviation (SD) of age, weight, height, and body mass index (BMI).

| Group | N | Mean±SD of | Mean±SD of | Mean±SD of | Mean±SD of |
|---------|----|------------|-------------|------------|------------|
| | | age (year) | weight (kg) | height (m) | BMI |
| Tai Chi | 15 | 67.16±4.04 | 60.91±8.10 | 1.55±3.90 | 25.01±2.57 |
| Pilates | 15 | 66.50±2.93 | 59.58±5.83 | 1.56±5.58 | 24.42±1.99 |
| Control | 15 | 67.50±4.66 | 65.66±9.94 | 1.55±5.35 | 27.15±3.06 |

Table 1. Mean and SD of age, weight, height, and BMI of participants

Table 2. Results of one-way ANOVA of descriptive variables

| Statistical | Sum of squares | df | Mean | F | Sig. |
|----------------------|----------------|----|-----------|-------|-------|
| indicators | | | squares | | |
| Source of variations | | | | | |
| Age | 6.22 | 2 | 3.11 | 0.20 | 0.820 |
| Height | 6.22 | 2 | 3.11 | 0.124 | 0.884 |
| Weight | 245.38 | 2 | 122.69 | 1.85 | 0.173 |
| BMI | 49.74 | 2 | 24.87 | 2.73 | 0.134 |
| Simple RT | 4756.533 | 2 | 2377.267 | 0.466 | 0.630 |
| Selective RT | 24011.511 | 2 | 12005.756 | 1.607 | 0.213 |

According to Table 2, results of the ANOVA test and its insignificance (P<0.05) in all measurement variables, individuals have been assigned to three groups homogeneously.

Table 3. Mean and standard deviation of participants' scores in simple and selective RT within pretest and posttest stages

| Test | Pretest (Mean±SD) | | Posttest (Mean+SD) | | |
|------------------|-------------------|--------------|--------------------|--------------|--|
| Statistic | Simple RT | Selective RT | Simple RT | Selective RT | |
| Tai Chi exercise | 620±72 | 1009±111 | 564±46 | 912±67 | |
| Pilates exercise | 598±65 | 958±75 | 540±83 | 871±53 | |
| Control | 606±70 | 1004±65 | 567±70 | 986±77 | |

Table 3 reports the mean value and standard deviation of participants' scores in simple and selective RT variables within pretest and posttest stages.

| Variable | Group | Sig. (pretest) | Sig. (posttest) |
|--------------|---------|----------------|-----------------|
| Simple RT | Tai Chi | 0.364 | 0.120 |
| | Pilates | 0.850 | 0.065 |
| | Control | 0.089 | 0.705 |
| Selective RT | Tai Chi | 0.173 | 0.621 |
| | Pilates | 0.522 | 0.285 |
| | Control | 0.313 | 0.109 |

Table 4. Results of Kolmogorov-Smirnov test of variables in pretest stage

According to Table 4, all studied variables were insignificant in the Kolmogorov-Smirnov test within pretest and posttest sages (P<0.05). Hence, all variables had a normal distribution.

Table 5. Results of composite ANOVA with repeated measurement of simple RT between groups

| Statistical | Sum of | df | Mean | F | Sig. | Eta |
|----------------------|-----------|----|-----------|--------|--------|---------|
| indicators | squares | | squares | | | squared |
| | | | | | | |
| Source of variations | | | | | | |
| Stage | 32947.600 | 1 | 32947.600 | 32.187 | 0.0001 | 0.434 |
| Stage * group | 15981.667 | 2 | 7990.833 | 7.806 | 0.001 | 0.271 |
| Error (stage) | 42992.733 | 42 | 1023.637 | | | |
| Group | 13475.400 | 2 | 6737.700 | 0.780 | 0.465 | 0.036 |

As reported in Table 5, the main effect of the stage (P<0.05) and interactive or mutual stage*group effect (P<0.05) were significant in the simple RT test. Accordingly, the three groups showed a significantly different performance in the simple RT test. Figure 1 depicts the different effects between three studied groups in terms of simple RT test scores. As it is seen, there was a minor difference between groups in the pretest, and the control group had the shortest simple RT (598.4). On the contrary, the difference between the two training

groups was greater than the control group in the post-test stage. The Pilate's group obtained the lowest mean value (540.66).

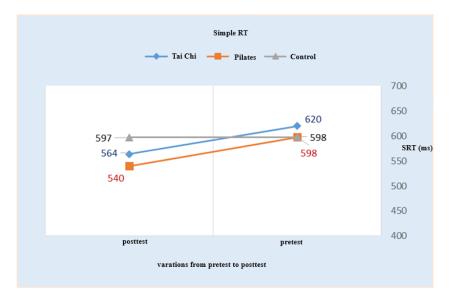


Figure 1. Mean scores of SRT among three groups in pretest and posttest

According to ANOVA results, there was a significant difference (P<0.0005) between the three studied groups regarding the SRT test. Tukey's post hoc test was used to determine the source of difference, and results were reported in Table 6.

Table 6. Results of Tukey's post hoc test to determine the source of difference between three groups in SRT posttest

| Statistical indicators Source of variations | Mean differences | Standard error | Sig. |
|---|---------------------|-------------------|-------|
| Groups 1 & 2 | 23.866 | 24.676 | 0.999 |
| Groups 1 & 3 | -33.266 | 24.676 | 0.555 |
| Groups 2 & 3 | -57.133 | 24.676 | 0.077 |

*group 1" Tai Chi exercise, group 2: Pilates' exercise, group 3: control

According to table 6, there was no significant difference between Tai Chi and Pilates' exercise groups, Tai chi and control groups, and Pilates and control groups (P>0.05). As seen in Figure 1, the Pilates group had the lowest mean score of SRT in pretest (598.4) and posttest (540.66). The Tai Chi group obtained pretest and posttest scores of 620.47 and 564.53, respectively.

| Table 7. Results of composite ANOVA with repeated | measurement of selective RT between groups |
|---|--|
|---|--|

| Statistical | Sum | of | df | Mean | F | Sig. | Eta |
|-------------|---------|----|----|---------|---|------|---------|
| indicators | squares | | | squares | | | squared |
| | | | | | | | |

| Source of variations | | | | | | |
|----------------------|------------|----|------------|--------|--------|-------|
| Stage | 101069.511 | 1 | 101069.511 | 53.999 | 0.0001 | 0.562 |
| Stage * group | 27894.822 | 2 | 13947.411 | 7.452 | 0.002 | 0.262 |
| Error (stage) | 78611.667 | 42 | 1871.706 | | | |
| Group | 97774.867 | 2 | 48887.433 | 4.860 | 0.013 | 0.188 |
| Error | 422450.733 | 42 | 10058.351 | | | |

As reported in Table 7, the main effect of the stage (P<0.05), group (P<0.05), and interactive or mutual stage*group effect (P<0.05) were significant in the selective RT test. Accordingly, the three groups showed a significantly different performance in the selective RT test. Figure 2 depicts the different effects between three studied groups in terms of selective RT test scores. As it is seen, there was a minor difference between groups in pretest and Pilates' group had the shortest selective RT (958.07). On the contrary, the difference between the two training groups was greater than the control group in the post-test stage. The Pilate's group obtained the lowest mean value (871.60).

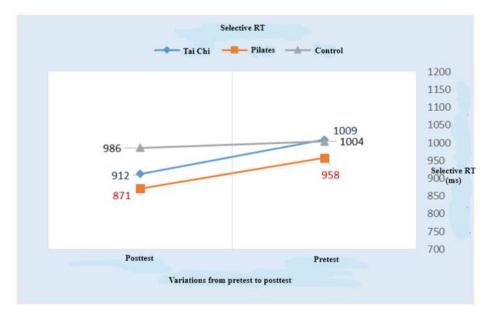


Figure 2. Mean scores of Selective RT among three groups in pretest and posttest

According to ANOVA results, there was a significant difference (P<0.005) between the three studied groups in the selective RT test. Tukey's post hoc test was used to determine the source of difference, and results were reported in Table 8.

Table 8. Results of Tukey's post hoc test to determine the source of difference between three groups in selective RT posttest

| Statistical indicators | Mean | Standard | Sig. |
|------------------------|-------------|----------|------|
| | differences | error | |
| Source of variations | | | |
| | | | |

| Groups 1 & 2 | 41.000 | 24.378 | 0.300 |
|--------------|----------|--------|-------|
| Groups 1 & 3 | -73.866 | 24.378 | 0.013 |
| Groups 2 & 3 | -114.866 | 24.378 | 0.001 |

*group 1" Tai Chi exercise, group 2: Pilates' exercise, group 3: control

According to table 8, there was not any significant difference between Tai Chi and Pilates' exercise groups, while there was a significant difference between Tai Chi and control groups, Pilates and control groups (P<0.05). As seen in Figure 2, Pilates' group had the lowest mean score of selective RT test in pretest (958.4) and posttest (781.60), which were significantly different from control group scores. The Tai Chi group obtained pretest and posttest scores of 1009.60 and 912.60, respectively, which were lower than the mean values of the control group. There was no significant difference in the control group from pretest (1004.18) to posttest (986.47).

Discussion and Conclusion

The purpose of the extant study was to compare the effects of 1week Pilates and Tai Chi exercises on simple and selective reaction time among patients who have Parkinson's disease referring to the rehabilitation center for older people in Qom County. The results indicated no significant difference between the effects of Pilates and Tai Chi exercises on SRT. The main effect of stage and interactive or mutual stage*group effect was significant in the SRT test. Accordingly, the three groups showed a significantly different performance in the SRT test. In the posttest stage, the difference between the two training groups was greater than the control group, and the Pilates group obtained the lowest mean value. The most important reason for the lack of difference between SRTs of training group may stem from the genetic attribute of SRT and is a kind of motor ability. The pre-motor part's SRT is not long since it requires less response selection and neural processing procedures. Christina and Rose (1985) reported that reaction time changes were caused by increasing stimulus complexity leading to increased premotor time. Therefore, the exercise had an effect, but this effect was not statistically significant so that the effect of any exercise was not significant on the simple reaction time compared to selective RT.

The results of the extant study showed a significant difference between Pilates and Tai Chi exercises in terms of their effects on selective reaction time. Three studied groups indicated significantly different performances in the selective RT test. There was a low difference between pretest scores of groups, and Pilates' group had the shortest selective reaction time. The difference between the two training groups was greater than the control group in the posttest stage, and the Pilates group obtained the lowest mean value among the three groups. Few behavioral studies have shown the major motor defects in the early stages of Parkinson's disease compared to individuals in the control group. A study showed that PD patients showed impaired upper limb movements, including writing, pointing, and aiming tasks, compared to the control group's individuals.

Contrary to the control group, PD patients performed an aiming task slower while moving towards the target compared to the case moving beyond a target. Furthermore, PD patients showed lower accuracy in pointing tasks than the control group (Ponsen et al., 2008). RT task in the extant study was similar to the aiming task with motor time importance. Researchers also studied complex upper limb motor function and found that PD patients could not illustrate a circle with two hands compared to control groups (Ponsen et al., 2008).

Pfann et al. (2001) found that PD patients had some motor impairments and abnormalities in muscles activations during simpler tasks, such as rapid elbow flexion movements over a wide range of distances compared to control groups. This study showed lower velocity of elbow movements in PD patients than the control group's individuals, so that PD patients had less ability while increasing movement distance, which reduces movement

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balance velocity. Electromyography (EMG) data analysis indicated that PD patients had certain limits n modulating agonist movement while responding to the task requirements, and the antagonist movement schedule in patients with severe disease was accompanied by more impairments. All of the mentioned reasons reduced the reaction time of PD patients. Montgomery et al. (2000) studied the mild symptoms of idiopathic Parkinson's disease (iPD) by using some tests. In the case of motor function tests, patients bent and opened their writs for different targets, and movement velocity was recorded. Movement limits were shown in a set of motor tasks, such as bending and opening elbow, writs, and catching force control.

Beste et al. (2009) found that event-related potential (ERP), the error negativity was considerably lower in PD patients compared to control groups. Pierantozzi et al. (2001) used TMS and found that early and late MEP inhibition was significantly reduced in PD patients compared to health respondents. This abnormal inhibition may be reversed with Apomorphine¹, administration Dopamine receptor agonist, indicating that cortical and subcortical loss of dopaminergic transmission in PD patients is associated with impaired motor cortical inhibitory mechanisms in the early stages of Parkinson. Cantello et al. (2007) used TMS and concluded that PD patients showed long-latency cortical inhibition compared to the control group's individuals. The pathologic enhancement of latency cortical inhibition was seen in PD patients in late stages, which found the role of pathology in abnormalities of continuous and rapid voluntary movements in PD (Berardelli et al., 1996). Many studies have shown the positive effect of sports exercises on motor symptoms of PD, including motor function, doing daily activities, improved balance, and flexibility (Shen et al., 2016; Schlenstedt et al., 2015; Alves et al., 2015; Rosenthal & Dorsey, 2013). Many studies have found the important role of physical activity level in determining RT. Spirduso carried out an interesting study to compare RTs in four groups of active and sedentary young and older men. Spirduso found that active older men and sedentary young men had similar RT, while there was a considerable difference between RTs of active and sedentary older men (Gallahoo & Ozmon, 2005). Physical activity improves metabolism, respiration, blood circulation, digestion, and the function of external secretory glands. The increased blood circulation in the central nervous system (CNS) is necessary for the lifespan of brain cells and information processing efficiency.

Moreover, physical activity improves the function of some cerebral peduncles. These factors have a positive effect on central areas of RT. The increased blood circulation in the lower extremities produces sufficient temperature for rapid conduction of nerve impulses to muscles affecting the more peripheral parts of RT. Spirduso explains that lack of physical activity may cause CNS dysfunction due to the increased effects, blood pressures, and higher pigment density (Gallahoo & Ozmon, 2002). Inaccuracy of participants' reports while filling out the questionnaires, mental and psychological conditions of participants, and lack of control over their diets were some constraints of the present study. This study was conducted on men; hence, it is recommended to study women in further research. Moreover, larger samples can be used in further studies to expand the results' generalization.

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¹ A crystalline substance derived from morphine.

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