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Aerobic Neural Priming Intervention for Sub-Acute Ischemic Stroke: A Case Study

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Abstract:

Background: Neural priming refers to a change in the neurologic system which is induced by a paired, preparatory stimulus. Various priming strategies have been explored, with particular promise for aerobic activity as a safe, low cost, and high-yield option. This concept has been attractive in the field of rehabilitation post neurological insult with the intention to optimize functional recovery through enhanced neuroplasticity. **Intervention:** In this case study, the patient participated in moderate-intensity aerobic exercise immediately prior to skilled physical therapy 3 times per week for 2 weeks (6 bouts) as a function of his inpatient rehabilitative intervention. **Case Description:** The patient was a 52-year old male with a recent infarction of the posterior inferior cerebellar artery (PICA) territory. **Setting:** The inpatient rehabilitation clinic is an 18-room, hospital-based unit in the Midwest that specializes in neurologic rehabilitation. Patients receive 3 hours of therapy 5 days/week, which is shared between physical therapy, occupational therapy, and speech therapy. **Outcome measures:** 10 meter walk test (10 MWT), Smart Balance Master (SBM) assessment, video recording, and a clinical assessment of function were documented during this case study. **Results:** Gait speed, balance, independence with functional mobility, and ambulation tolerance improved during the 2-week period. **Purpose:** This document describes the administration, barriers, and results of the intervention, which may serve as a valuable reference tool for clinicians, patients, and/or researchers.

Background and Purpose:

Restorative strategies in physical neurologic rehabilitation are largely centered around concepts of activity-based neuroplasticity. Rehabilitation specialists prescribe specific movement patterns to promote functional recovery at a cellular level. Neurogenesis, synaptogenesis, and pruning are physiological processes that can be biased to improve movement efficiency, strength, coordination, and endurance. Neural priming has been explored as a viable restorative approach to optimize plasticity within the motor system[1]. Priming can be described as altering the change in a behavior by applying a stimulus immediately prior to the task. Various methods have been examined, including transcranial magnetic brain stimulation, motor imagery, pharmaceuticals, and sensory nerve activation. Priming the motor system with aerobic activity is a systemic, low risk[2], and cost-effective option that has gained particular interest in the field of neurorehabilitation[1,3].

Although the mechanism of aerobic neural priming is almost certainly multi-dimensional, many contemporary models revolve around the effects of brain-derived neurotrophic factor (BDNF). Literature suggests that this neurotrophin is important for long term potentiation, neuronal protection, differentiation, and synaptogenesis[1,4]. Beyond the cellular level, BDNF has been associated with learning and improved performance in animal models[5,6]. It has been demonstrated that an acute bout of aerobic exercise can increase serum BDNF for up to 60 minutes post-activity[4]. Other models for aerobic priming include increased cortical excitability, modified activity of neurotransmitters (serotonin, dopamine, etc.), and increased cerebral blood flow[1,4,7]. These findings have prompted the theory that a dose of cardiovascular conditioning immediately prior to a targeted rehabilitative intervention will stimulate motor learning.

Despite the surge of interest on this topic, documented evidence of aerobic neural priming is currently very limited. Mang, et al. demonstrated that a short bout of high-intensity exercise increased BDNF 3.4 fold and improved the temporal tracking of a joystick-based continual tracking task immediately following the activity[4]. With a similar experimental model, Roig, et al. showed that a short, intense bout of aerobic priming improved long-term retention of a visuomotor tracking task[8]. In another study, Statton, et al. evaluated the effects of moderate-intensity aerobic priming[9]. This group discovered improved motor skill acquisition with an isometric squeezing task, although there was no significant difference in retention. It should be acknowledged that each of these studies were performed with young, healthy adults and it is possible that other populations would respond differently.

In addition to the potential impact on motor learning, aerobic conditioning also has global health benefits that are particularly relevant to patients suffering from neurologic lesion[3,10]. It is known that individuals who have experienced one stroke are more likely to have a recurrent stroke; this emphasizes the importance of physical activity as a preventative measure[3]. Aerobic exercise also has the potential to improve cognitive function and quality of life (QOL), which are often impacted from a cerebrovascular accident[3,4]. Despite the established benefits of aerobic conditioning, stroke patients often fall well below the recommended 150 minutes of moderate-intensity exercise/week by the American College of Sports Medicine. As one example, a longitudinal study found that stroke survivors spend an average of just 3 minutes per physical therapy session and 1 minute per occupational therapy session above 60% maximal heart rate (MHR)[11].

Priming the neuromotor system is a relatively modern concept and interest for aerobic activity as a stimulus is growing in the scholastic community. Barriers to large-scale studies include the uniqueness of each patient, practicality, and the multivariate nature of the intervention (timing of the primer, intensity, frequency, etc). Furthermore, there is a great void in literature evaluating clinical application to specific patient populations[1]. The primary purpose of this case study is to describe the use of aerobic priming as a rehabilitative treatment option for PICA infarction in the inpatient rehabilitation setting. The secondary purpose is to record changes in this patient’s function over a 2-week period, which may have been influenced by neural priming coupled with traditional rehabilitation interventions.

Patient History and Systems Review:

The subject of this case study was a 52-year old male from rural Iowa with significant medical history of hyperlipidemia, hypertension, pre-diabetes, and tobacco use (80 pack year history). He was 5'7", weighed 151 pounds, lived a fairly sedentary lifestyle, and he worked full-time as a truck driver. He was independent for all activities of daily living and job responsibilities prior to the stroke. The patient began experiencing dizziness, nausea, left-sided weakness/clumsiness, and facial numbness on the day following a fall. He went to the hospital where clinicians recognized horizontal nystagmus, non-stop hiccupping, loss of pain/temperature on the right side of the body, and a left postural lean. Despite motor and sensory impairment, there was no pain or detectible change in cognition. The healthcare team recognized symptoms consistent with Wallenberg Syndrome (lateral medullary syndrome). An MRI revealed foci of acute infarction which were believed to have originated from a small lesion to the vertebral artery during the fall. Involved structures included the left lateral medulla oblongata, the vermis, and the left cerebellar hemisphere along the PICA territory. The patient stayed three days in acute care and was referred to inpatient rehabilitation (four days post fall).

Clinical Impression #1:

At this point in the clinical decision making process, there were a number of reasons why neural priming via aerobic exercise was considered for this individual. Per chart review, he had a body mass index within normal range, he was relatively young, and he did not have severe impairment. These findings suggested improved capacity to achieve and sustain moderate-intensity aerobic exercise. In addition, the prophylactic nature of aerobic conditioning could be particularly beneficial to this patient because he is relatively young. He also did not have any comorbidities that directly contraindicated moderate-intensity aerobic conditioning and he was cognitively unimpaired, which decreases communication barriers and gives more merit to measures such as rating of perceived exertion (RPE). Finally, Mang, et al. found improved temporal precision with an aerobic neural priming intervention[4]. Therefore, the group argued that individuals with cerebellar dysfunction (who frequently struggle with motor sequencing) could generate distinct profit from this type of intervention. Overall, this patient was considered appropriate because he was able to provide credible verbal feedback, he was reasonably low-risk for an aerobic intervention, and he demonstrated a good capacity for functional improvement.

Examination:

The examination was separated because it took two sessions to record all baseline data. Due to time constraints, this practice is not uncommon in the inpatient rehabilitation setting. Part 1 was recorded on the Friday of his admission and part 2 was recorded on Monday, the following date of therapy. It is noteworthy to distinguish the data points in this case study because functional change was noted between the two examination dates.

Part 1: The patient was questioned over home environment, prior level of function, and life roles on the first visit. Gross motor/sensory systems, cognition, and functional mobility were also assessed. Manual muscle testing was utilized for an estimate of strength and it was determined that this patient did not have any functional strength impairments. A coordination screen of upper and lower extremities exposed impairment of the left side. The patient's mobility was assessed and he required a front-wheeled walker and minimal-moderate (~25-50%) physical assist of a skilled therapist to remain upright when transferring from one sitting surface to another. For gait, the individual required minimal-moderate assistance of two therapists for safety and demonstrated uncoordinated stepping with his left lower extremity. Due to the required assistance with ambulation, the patient utilized a manual wheelchair as his primary mode of mobility. In static upright position, the patient required constant moderate (~50%) physical assistance to keep from falling to the left.

Following initial evaluation, it was determined that this patient would benefit from 90 minutes of physical therapy and 90 minutes of occupational therapy 5 days/week (the rehabilitation team decided that he did not need speech therapy). The physician was consulted and he agreed that this individual was a low-risk candidate for moderate-intensity aerobic activity. The patient gave verbal and written consent to participate in the case study and gave approval to use video recording as another mechanism of functional status assessment. Finally, he reported that his goals were to be safe for his return to home, to phase out reliance on the wheelchair, and to progress toward return to work.

Part 2: The patient participated in a 10 MWT, a "Sensory Organization Test" utilizing the SBM by NeuroCom®, and he was filmed ambulating a short distance. The patient's ambulation speed was 0.31 m/s per the 10 MWT, his balance scored 47% below the norm on the SBM, and a video of his gait can be found here (hyperlink to: https://youtu.be/oMFiu7CwXXk).

Refer to Figure 1 for a reference image[12] of the SBM. The subject stood in a mock visual environment on dual force plates. In this device, both the surface (force plates) and surround had dynamic capabilities. The Sensory Organization Test creates a composite, objectified balance score by measuring deviations of center of mass under 6 different conditions: 1) eyes open with stable surround and surface 2) eyes closed with stable surround and surface 3) eyes open with variable surface and stable surround 4) eyes open with stable surface and variable surround 5) eyes closed with variable surface 6) eyes open with variable surface and surround.

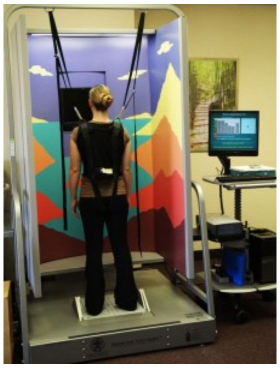

Figure 1: SBM device with the monitor which allows the instructor to visualize center of mass and modify settings.

Clinical Impression #2:

The examination further supported this patient's propriety for aerobic neural priming. Safety is a priority in health care and the physician's endorsement for the intervention was a valuable step toward assured well-being. Furthermore, the patient demonstrated significant impairment at baseline. One example was his preferred walking speed of 0.31 m/s per the 10 MWT. According to the Rehabilitation Measures Database, the average speed for his age is 1.39 m/s and the average for ambulatory stroke patients is 0.84 m/s[13]. Additionally, speeds less than 0.4 m/s are more likely to be limited to household mobility. Another indication of motor dysfunction was his score of 47% below average on the SBM. This affirmed that the patient was below average on multiple accounts and was thus a strong candidate for enhanced motor learning through a neural priming strategy.

It was determined that there would be two primary outcome measures for this intervention: 10 MWT and the SBM assessment. These were selected because gait speed and balance are relevant to the patient's goals and they can represent relative risk of falling. Secondary comparisons can be made between initial and post video recordings as well as qualitative assessment of functional status. Information gathered from a functional assessment is invaluable to the skilled clinician and further supported the case that this patient is appropriate for this intervention.

Intervention:

As mentioned earlier, the patient received 2 hours of rehabilitative therapy, 5 days per week, which is typical of standard inpatient rehabilitation units in the United States. Time was split equally between physical therapy and occupational therapy for this individual. He performed a 60-minute session of physical therapy in the morning and a 30-minute session in the afternoon to achieve his total requirement of 90 minutes per day. The aerobic priming intervention for this case study took place during scheduled physical therapy sessions in the morning at a frequency of 3 days per week for 2 weeks. The following describes a general framework of the intervention: the patient would arrive to his scheduled session, perform 15 minutes of aerobic conditioning, and then spend the remaining time with a skilled physical therapy intervention. This resulted in 3 hours/week (out of the 7.5 hours/week of physical therapy) directly performing an aerobic priming strategy.

The acute bout of aerobic activity was performed on a recumbent elliptical cross trainer. More traditional forms of aerobic conditioning such as biking or treadmill training require the exerciser to maintain upright posture and thus, would have been inappropriate for this patient. Moreover, the recumbent elliptical cross trainer was a comfortable and tolerable mode to challenge the cardiovascular system for a prolonged period of time. Intensity of aerobic priming was measured with RPE and heart rate. Moderate intensity activity is the equivalent of an RPE of 12 to 14 and approximately 60% of age-predicted MHR: Percent x (220-age) = [0.6 x (220-52)] = 100 beats/minute. Heart rate and RPE were recorded at baseline, at 5 minutes, at 10 minutes, and at 15 minutes to ensure proper intensity. Blood pressure was recorded at baseline to get an initial depiction of the cardiovascular system and at 15 minutes to assess response to physical activity. If blood pressure values deviated from normal, the intervention would be terminated or modified appropriately.

A physical therapy intervention immediately followed the aerobic priming. In an effort to keep the intervention clinically reasonable, the physical therapy prescription was not kept uniform. This allowed the physical therapist to execute a comprehensive, flexible, and progressive treatment that was subject to individual and day-to-day variance. The prescription included gait training, postural re-education, and tasks challenging balance and coordination. Verbal education was also provided throughout the plan of care reviewing activity modification, coordination strategies, and pathological implications of his stroke to the movement system.

Skillful progression is crucial to rehabilitation and was implemented in multiple ways during this intervention. Aerobic priming was advanced as physiologically appropriate to maintain the target intensity of 12-14 on RPE and 60% MHR. Level of resistance and steps per minute were periodically adjusted on the recumbent elliptical cross trainer to stay within proper ranges. The physical therapy intervention was progressed at the discretion of the physical therapist and thus reflects standard practice. Rudimentary examples of clinical progression strategies are provided below:

(1) Balance:
- Static standing → static standing with decreasing base of support → dynamic standing (reaching, weight shifts, etc.) → dynamic standing with decreased base of support
- Hard surface → soft surface → variable surfaces

(2) Gait:
- Front wheeled walker → large-based quad cane → small based quad cane → single point cane → no assistive device
- Decreasing level of physical assistance provided by therapist
- Unidirectional ambulation on level surface → adding direction changes → adding obstacles

(3) Posture:
- orientation to midline in sitting → quadruped position → kneeling → tall kneeling → standing → dynamic upright posture (gait, marching, etc.).
- Assuming midline posture with eyes open and visual feedback (mirror, SBM, etc.) → eyes open without visual feedback of self → eyes closed

Task difficulty was also increased with distraction, decreasing amount of cues, performing tasks in an open environment, and asking the patient to complete the skill while fatigued.

In addition to physical therapy, the patient received 90 minutes of occupational therapy 5 days per week and assistance from nursing staff in the hospital room. He was also encouraged to perform exercises that were prescribed by the physical therapist during the day, particularly on weekends when he was not scheduled for therapy. These co-interventions are typical with the inpatient rehabilitation setting so they were not recorded as a function of this case study.

Outcome:

As discussed earlier, there were two primary outcome measures used to assess this individual: the 10 MWT and SBM assessment. These measures were chosen because they are directly related to the patient's dysfunction and his goals. In addition, the SBM records center of mass measures that could be utilized as visual feedback for the patient (provided as a printout following the assessment). The two measurements also complement each other, as the 10 MWT is a dynamic ambulatory assessment and the SBM provides a direct measure of balance in a static, upright position.

According to the Rehabilitation Measures Database, the 10 MWT has excellent (correlation coefficient greater than 0.75) test retest, interrater, and intra-rater reliability for stroke patients[13]. It is also categorized as excellent (correlation coefficient greater than 0.6) criterion validity and construct validity with the dynamic gait index, the functional gait assessment, and the berg balance scale[13]. These findings suggest that the 10 MWT is a consistent clinical tool and a good indicator for ambulatory function. The SBM has not been as extensively studied, but one group of researchers found a moderate-high (correlation coefficient greater than 60%) test-retest reliability and acceptable (greater than 10% predictive power) predictive validity with reference to ADL function 1-year follow up in stroke patients[14].

At baseline, the individual had a preferred walking speed of 0.31 m/s per the 10 MWT. After completing two weeks of inpatient rehabilitation, his preferred ambulation speed was 0.85 m/s. This speed is on par with the average for stroke victims (0.84 m/s) and places him in the category of those who are more likely to be unlimited community-level ambulators (greater than 0.8 m/s)[13]. Initially, he scored 47% below the norm with the SBM, which improved to 11% below normal at termination of the intervention. Although the score changed 36%, a reference for clinically relevant changes has not yet been determined for this test. For a qualitative overview of change in functional status, refer to table 1.

Table 1: Functional status assessment at admission and after the two-week intervention.

	Admission	Post 2-Week Intervention
Balance	• Static sitting: good • Dynamic sitting: fair • Static standing: fair • Dynamic standing: poor	• Static sitting: good • Dynamic sitting: good • Static standing: good • Dynamic standing: fair-good
Gait	• Minimal-moderate assistance of 2 therapists • Distance: 25' (terminated because not therapeutic) • Deviations: heavy left lean; left lower extremity with uncoordinated stepping • Assistive device: front wheeled walker. • Utilized a manual wheelchair for majority of mobility	• Contact guard assistance of one • Distances of 400'+ (community distances) • Deviations: slight medial/lateral sway which increases with long distances • Assistive device: single point cane • Did not require a wheelchair for any mobility
Bed mobility	• Modified independent (increased time) with sit to/from supine, rolling, scooting	• Independent with all bed mobility
Bed to/from chair transfer	• Minimal-moderate assistance of one therapist • Stand pivot transfer with front wheeled walker	• Close standby assistance of one • Ambulate to transfers with single point cane
Sit to/from stand transfer	• Minimal assistance • Requires front wheeled walker	• Close standby assistance • Assistive device not required
Sensation	• Impaired pain/temperature sensation on right side of body	• Unchanged

In addition to the formal outcome measures and the descriptive change in functional status, video was recorded on the first day of the intervention and on the last day of the intervention. Although the initial video was taken 3 days after admission, it gives valuable insight to the level of function at baseline. While video recording may be considered an unorthodox documentation method, the pre and post comparison provides valuable and functional observations. The initial video can be found in the "Examination" section of this document. Videos at completion of the intervention can be found here (hyperlink to: https://youtu.be/ndhwG7vGAB8) and here (hyperlink to: https://youtu.be/Zfzj1hI6O9w).

Discussion:

The scientific community has been supporting aerobic conditioning as a powerful asset to physical and mental health since the 1960's. Conversely, the biological framework for aerobic neural priming is in its infancy. Researchers are discovering that an acute bout of aerobic exercise temporarily stimulates increased BDNF, cerebral blood flow, and activity of neurotransmitters[1,4,7]. These physiological responses are associated with augmented motor learning and the transient nature suggests that timing of the paired behavior is an important variable. Applying this theoretical framework to patients who have experienced neurological insult is attractive to researchers and clinicians, alike. Although practitioners and the scholastic community share a common goal, a wide gap separates highly controlled laboratory findings from application to real-life, multi-dimensional patient populations. This intervention-based case study is a small step towards filling this void by illustrating the implementation of aerobic neural priming to traditional inpatient rehabilitation.

This case description includes the clinical decision making behind why the practitioners believed aerobic priming would be appropriate for this individual. In addition, a detailed report of the intervention was provided as a single example of how principles from aerobic priming could be applied to a stroke patient in the inpatient neurologic rehabilitation setting. Available research of priming has primarily evaluated performance/learning of a highly controlled, easily measured task. While this follows conventional experimental procedure, it detracts from clinical utility. In this case study, the physical therapy intervention that followed the aerobic stimulus was left to the discretion of the clinician. Judgment for appropriate intervention was based off of the needs of the patient with progression toward a safe discharge to home.

The patient experienced a significant improvement in functional status during his plan of care. His preferred walking speed improved from 0.31 m/s to 0.85 m/s – far surpassing the minimal clinically important difference of 0.14 m/s for the 10 MWT[13]. The individual's balance assessment also improved from 47% below average to 11% below average, as measured by the SBM. Although these results are encouraging, a clinically important difference has not been documented for this test so it is not appropriate to definitively conclude functional balance improvement. Additionally, the functional assessments describe multiple important improvements and progression towards his goals at initial evaluation. Examples include decreased required assistance for transfers, transitioning from a front wheeled walker to single point cane with gait, and increased ambulation distances.

It is not possible to measure the direct influence of aerobic priming on motor function with this case study. Numerous confounding variables undoubtedly influenced this individual's movement system including co-interventions, time, and the natural healing process. This being said, it should be acknowledged that this individual did not experience any adverse effects from the intervention, his function improved significantly (regardless of cause), and he made valuable progress toward improving the health of his cardiovascular system with aerobic conditioning. Therefore, this case study suggests that aerobic priming is a feasible treatment option for individuals suffering symptoms of a PICA infarction in a sub-acute setting.

The topic of aerobic priming warrants continued research, discussion, and clinical trials. Future studies should detail specific patient populations with clinically-relevant application methods. Additionally, cardiovascular assessment and response could be more controlled and assessed. For example, aerobic stress tests should be performed for more precise intensity prescription and data could be also be used to evaluate changes in the cardiovascular system. Future research could also apply aerobic priming to other rehabilitation settings (outpatient orthopedics, pediatrics, etc.) or evaluate optimal dosing for the priming. It is apparent that there are many factors to consider and much to be learned, but aerobic priming continues to show strong potential in the rehabilitation community.

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