



Manual of Procedures Summary of FLADEX project



Promoting Fitness & Health
through Physical Activity



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0. Abstract

Alzheimer's disease (AD) is one of the leading causes of disability worldwide. Alterations in cerebral blood flow (CBF) and blood biomarkers of AD are critical in the early stages of the disease. Exercise is a promising non-pharmaceutical intervention to reverse these physiological changes, but the specific mechanisms by which exercise improves brain health remain unknown. The flADex project aims to examine the acute effects of different types of exercise on CBF and blood biomarkers of AD in cognitively normal older adults.

FlADex is a counterbalanced crossover trial that will enroll 20 adults aged 68 to 83 years with negative brain amyloid status (<12 centiloid) who are non-carriers of APOE $\epsilon 4$. All participants will complete a 30-minute session of each condition in a randomized order: (i) moderate-intensity aerobic exercise (60–70% of maximum heart rate), (ii) moderate-intensity resistance exercise (perceived exertion rating: 4–6 points out of 10), and (iii) resting condition. The primary outcome, CBF, will be assessed using magnetic resonance imaging at baseline and at three post-condition time points (starting at 20, 27, and 34 minutes). Blood biomarkers of AD ($A\beta 42$, $A\beta 40$, p-tau217, p-tau181, GFAP, NfL) and growth factors (BDNF, IGF-1) will be measured before and after each condition (at 3, 50, and 70 minutes). Cognitive outcomes (sequential image memory and Flanker tests) and mood (POMS questionnaire and Feeling Scale) will be measured before and after the condition.

This document provides an index of the chapters detailing each of the manuals of procedures implemented in the flADex Project. The objective of publishing the flADex manuals of procedures is to enhance the visibility of the procedures conducted across all phases of the project and to make them openly accessible for consultation by anyone interested.

This document compiles all chapters and development protocols required for the implementation of the flADex Project:

Chapter 1. Ethics committee

Chapter 2. Logistics

2.1. Familiarization

Chapter 3. Recruitment, eligibility and screening

Chapter 4. Randomization and data management

4.1. Randomization

4.2. Data management

Chapter 5. Cognitive assessments and questionnaires

5.1. Cognitive assessments

5.2. Questionnaires

Chapter 6. Blood samples

Chapter 7. Magnetic Resonance Imaging (MRI) assessment

Chapter 8. Exercise intervention