Effects of Vitamin D Supplementation on Muscular & Cardiorespiratory Adaptations to Concurrent & Endurance Training in Mice

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IOWA SPACE NASA NASA GRANT CONSORTIUM

BACKGROUND

- Microgravity environments are associated with reductions in muscle strength and cardiorespiratory fitness (Cotter et al., 2015).
- These adverse effects are further exacerbated because astronauts are more likely to be vitamin D deficient due to inadequate sunlight and dietary changes (Carswell et al., 2018).
- Recent evidence suggests vitamin D stimulates muscle growth, supports optimal muscle function by regulating growth hormones, such as insulin-like growth factor 1 (IGF-1), fibroblast growth factor (FGF), and vascular endothelial growth factor (VEGF), and improves cardiorespiratory fitness (Dzik & Kaczor, 2019; Bartoszewska, Kamboj, & Patel, 2010).

BACKGROUND

CONCURRENT:

- To promote overall muscle health and cardiorespiratory fitness, individuals typically perform both strength and aerobic exercise (i.e. concurrent training) (Carrithers et al., 2007).

ENDURANCE:

- Vitamin D levels have been positively associated with endurance exercise performance (Carswell et al., 2018).
- Vitamin D supplementation has been shown to improve physical activity rates in those with deficiencies (Karefylakiset al., 2018).

PRIMARY HYPOTHESES

CONCURRENT: Vitamin D supplementation will positively impact the ability of skeletal muscle and the cardiorespiratory system to effectively respond to concurrent training evidenced by improved contractile function, cardiorespiratory fitness and growth factor levels compared to placebo.

ENDURANCE: Vitamin D supplementation will positively impact the ability of the cardiorespiratory and muscular systems to effectively respond to endurance training as evidenced by increased running wheel distance, maximal treadmill test time, and muscle endurance and strength.

METHODS

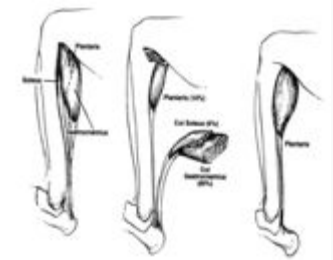
- **CONCURRENT:** Adult (3-4 months old), male C57 mice were divided into the following groups (n = 4-8/group):

Treatment	Activity
Placebo	Sham
	Strength (FO)
	Concurrent (FO & RW)
Vitamin D (0.5 µg/1 kg body weight)	Sham
	Strength (FO)
	Concurrent (FO & RW)

- **ENDURANCE:** Adult (3-4 months old), male C57 mice were divided into the following groups (n = 2-6/group):

Treatment	Activity
Placebo	Sedentary
	Running Wheel (RW)
Vitamin D (0.5 µg/1 kg body weight)	Sedentary
	Running Wheel (RW)

METHODS

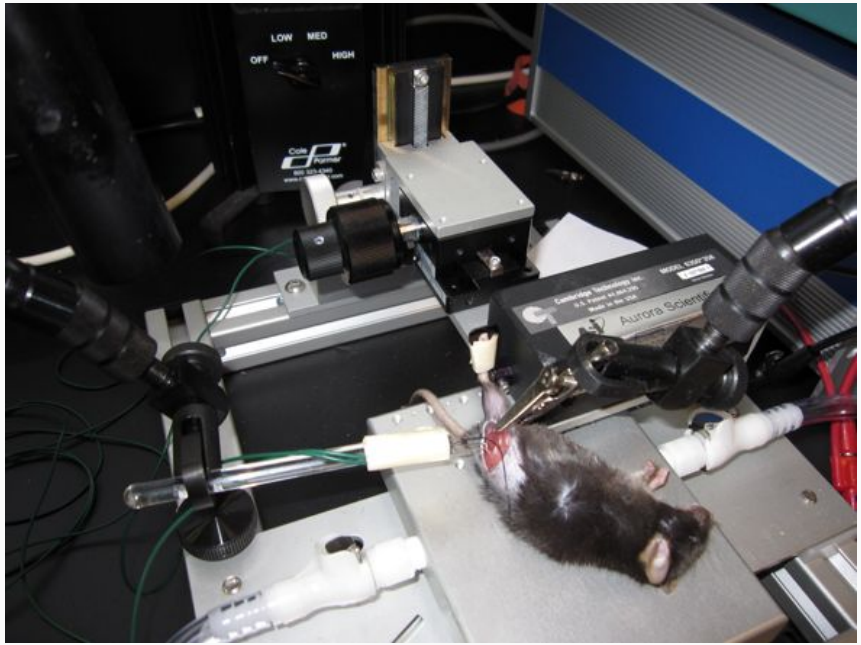


- **CONCURRENT ONLY:** Functional overload (FO) involves surgical removal of the soleus and gastrocnemius muscles to bilaterally overload the plantaris and mimic strength training.
- Maximal exercise tests were completed before and after 14 days of TM training or normal cage activity in sedentary groups.
  - Following a 5 min. warm-up, mice ran at 12 m/min and 5% grade and speed was increased 2 m/min every 2 min. up to 18 m/min. At 22 min. speed was increased 2 m/min every 2 min. until volitional fatigue.
- Overload/RW mice had unlimited running wheel (RW) access or remained sedentary.

METHODS

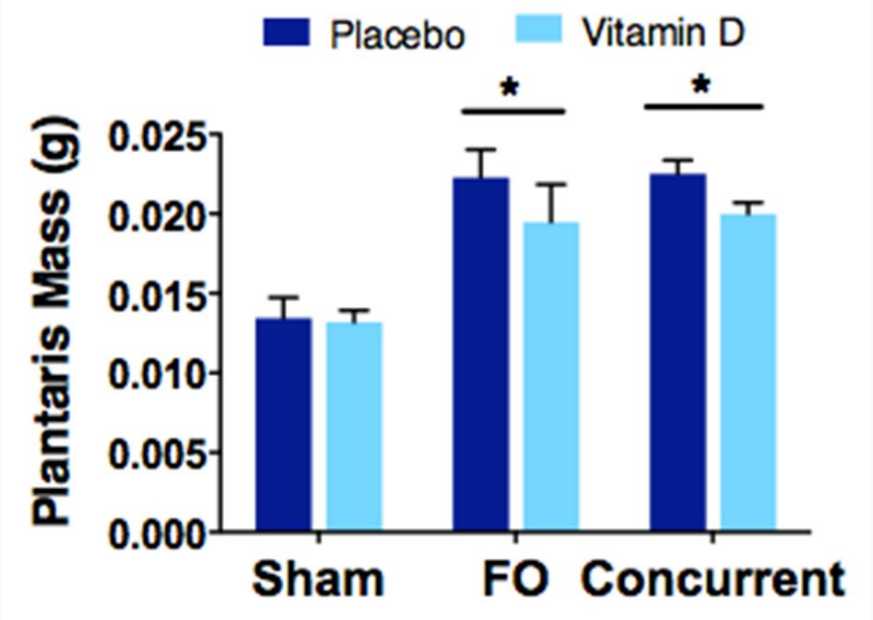
- Mice received daily vitamin D (0.5 μg/kg body weight) or placebo (saline) for 14 days following surgery.
- After 14 days, maximal isometric plantarflexor force and fatigue were measured in anesthetized mice with a dual-mode footplate system.
  - 10 contractions were evoked every 5 seconds by sciatic nerve stimulation.
  - Fatigue was calculated as the decline in force over 10 contractions relative to maximal force.
- IGF-1, FGF, IL-6, and VEGF levels were measured in muscle homogenates with ELISA assays

In Vivo Force Measurement

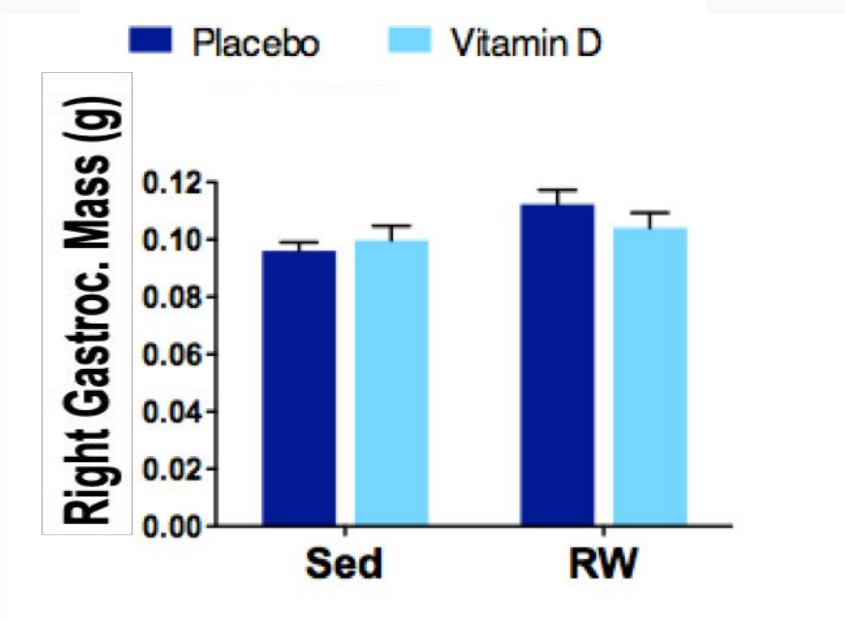


RESULTS - MUSCLE MASS

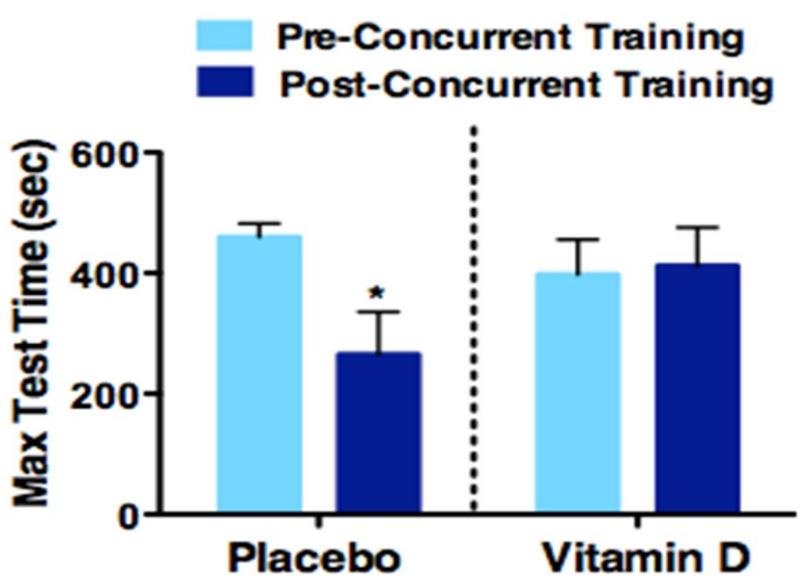
CONCURRENT

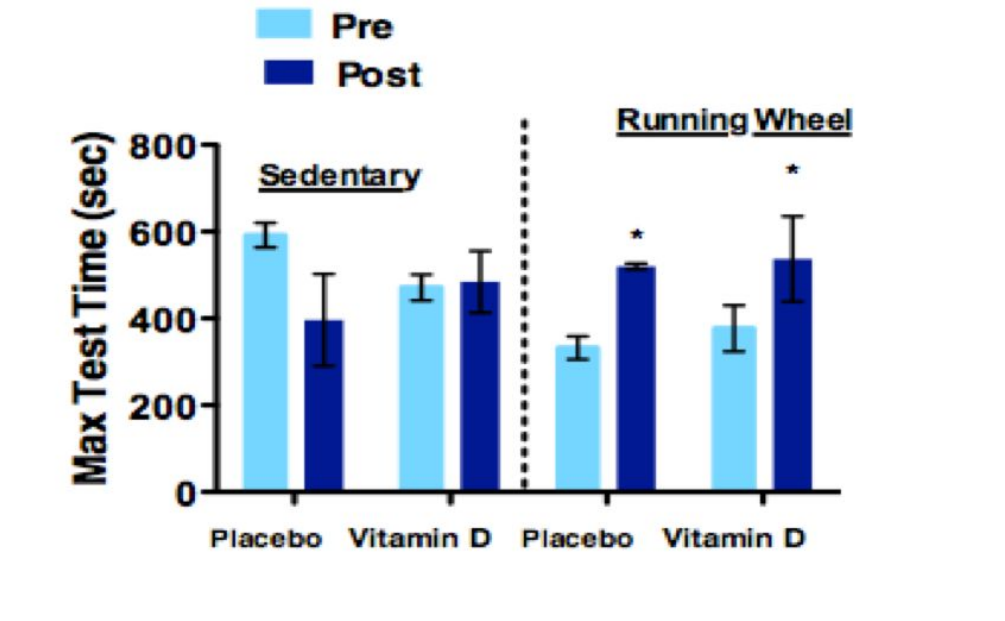


ENDURANCE



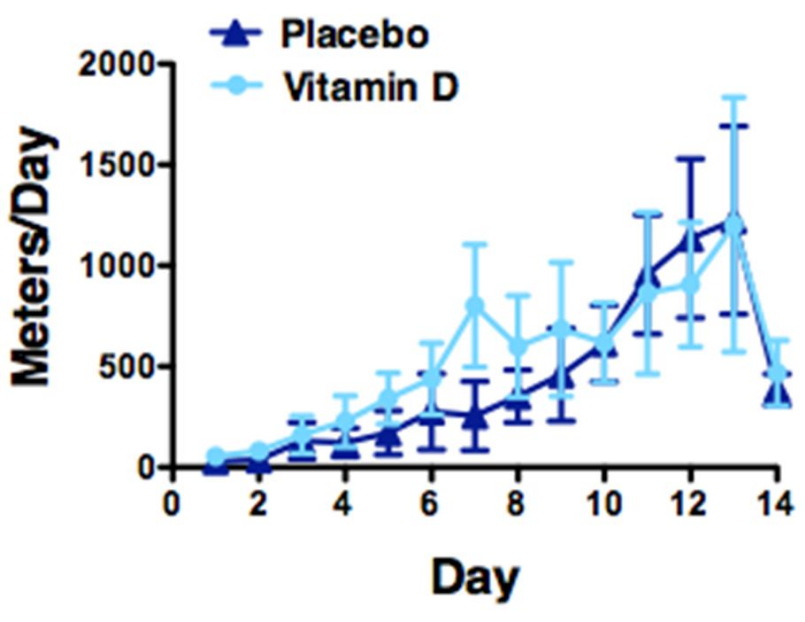
RESULTS - MAX EXERCISE TEST



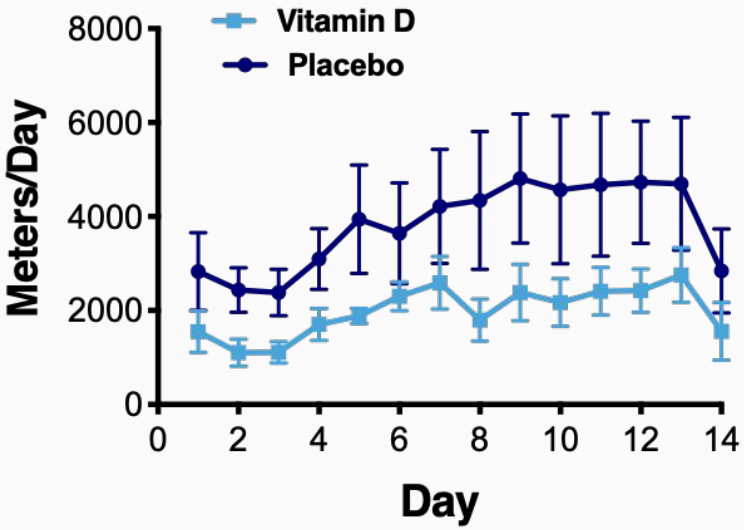


RESULTS - RW DISTANCE

CONCURRENT

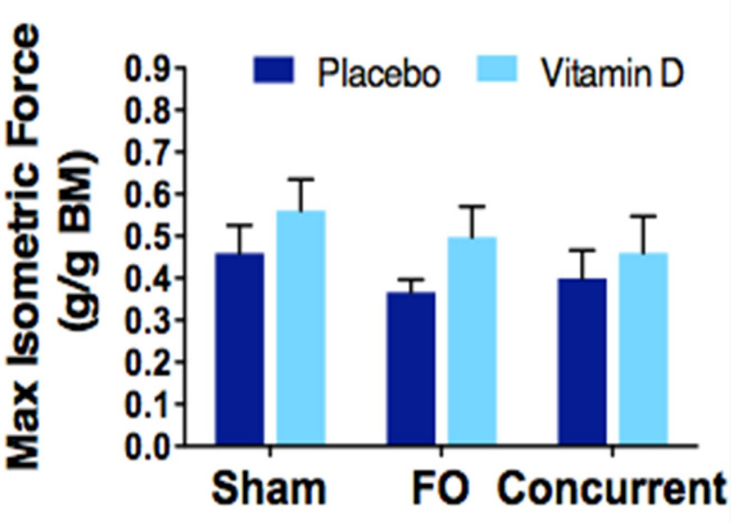


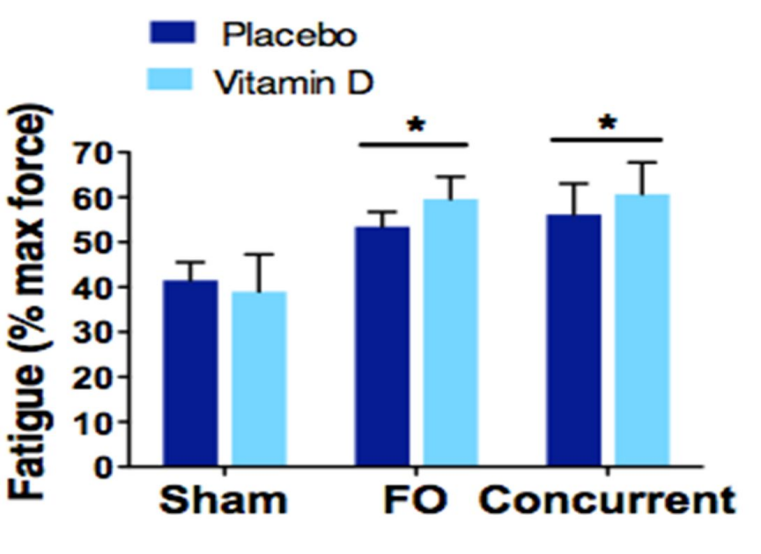
ENDURANCE



RESULTS - MAX FORCE & FATIGUE

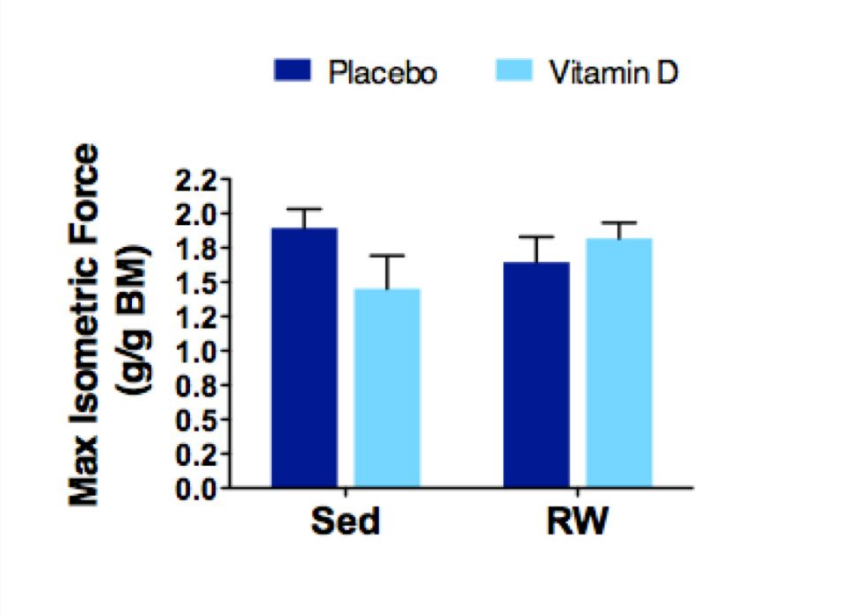
CONCURRENT

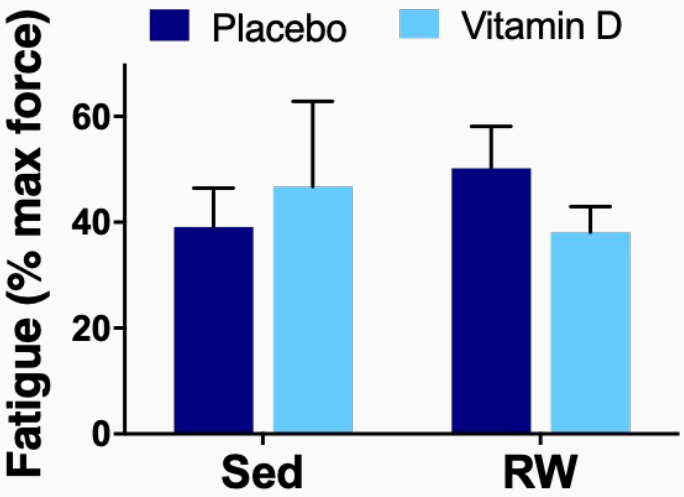




RESULTS - MAX FORCE & FATIGUE

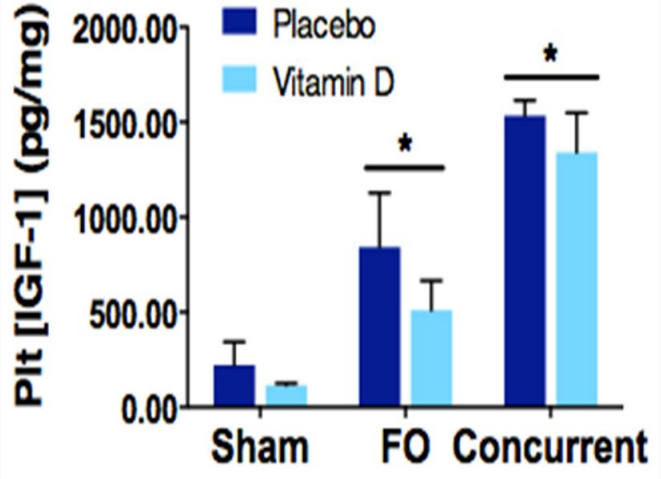
ENDURANCE

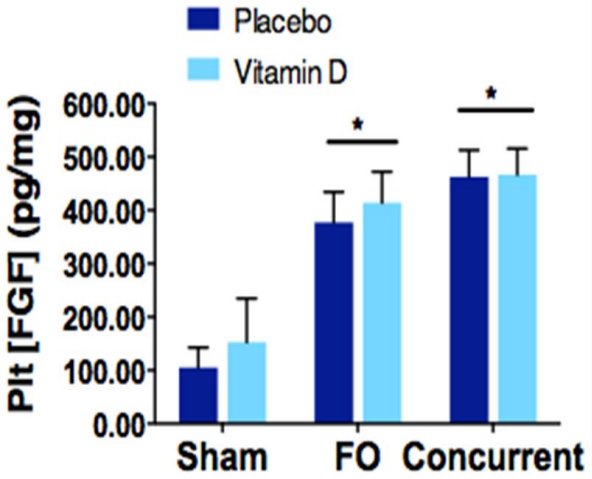


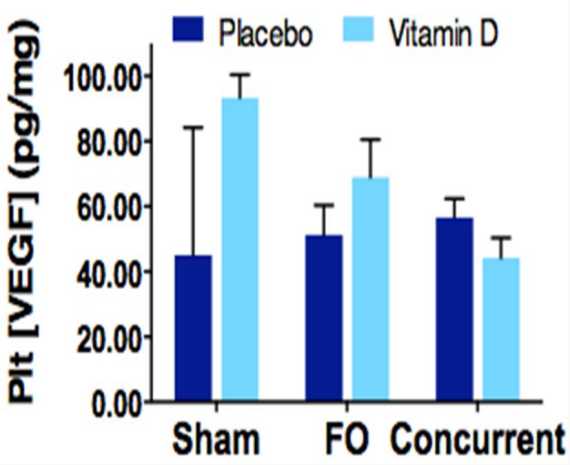


RESULTS - IGF-1, FGF, & VEGF

CONCURRENT

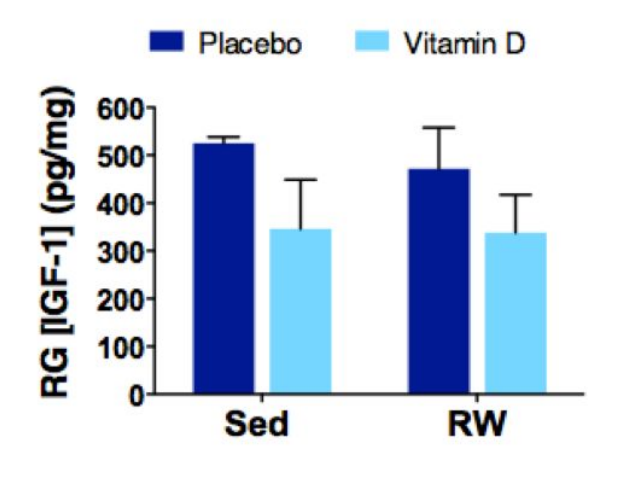


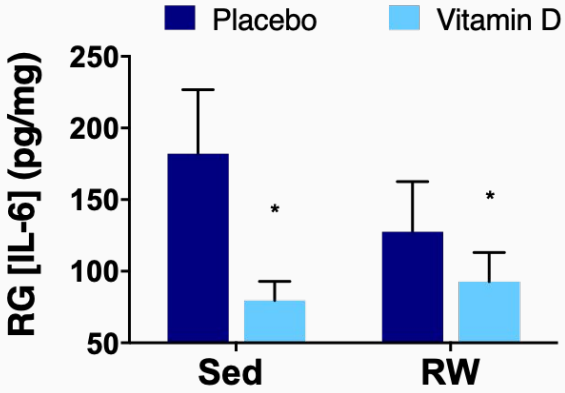


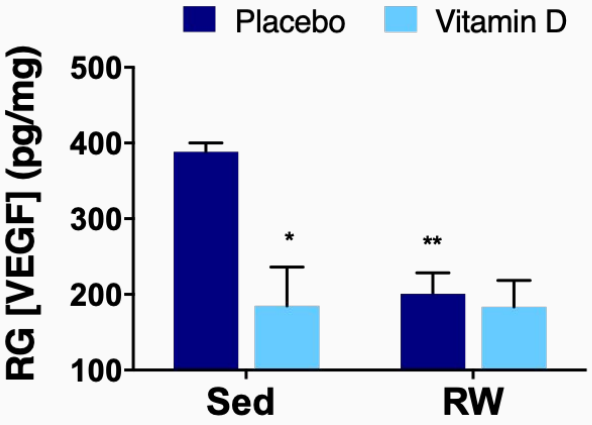


RESULTS - IGF-1, IL-6, VEGF

ENDURANCE







KEY FINDINGS

CONCURRENT:

- **Physiological Significance: Vitamin D improved the ability of the cardiorespiratory system to positively respond to concurrent training while vitamin D in combination with FO did not significantly enhance muscle hypertrophy**
  - No differences between strength and concurrent training in muscle mass and contractile function suggests the addition of aerobic exercise did not impair muscle hypertrophy or strength.
  - Provides a basis for future studies in humans to assess other types of dietary supplementation and exercise protocols that will provide the most effective therapy for astronauts prior, during, and post-mission to prevent muscular atrophy.

KEY FINDINGS

ENDURANCE:

- **Physiological Significance: Vitamin D did not improve the ability of skeletal muscle or the cardiorespiratory system to positively respond to endurance training.**
  - Observed differences between sedentary and RW groups were independent of treatment, suggesting that vitamin D supplementation did not enhance cardiorespiratory function.
  - Provides a basis for future studies in humans to assess various types of exercise and dietary supplementation that will provide the most effective therapy for astronauts prior, during, and post-mission to prevent muscular atrophy and deficiencies in cardiorespiratory function.

FUTURE RESEARCH

- Larger animal sample size or clinical trials and longer durations of supplementation (Karefylakis et al., 2018; Cotter et al., 2015; Singla et al., 2017; Scholten, Sergeey, Song, & Birger, 2015; Carrithers et al., 2007)
- Potential benefits vitamin D supplements have on immune and bone health, or other various long-term impacts (Carswell et al., 2018; Kouhnavard et al., 2014)
- Include both male and female subjects (Arazi, Samadpour, & Eghbali, 2018)
- Longer bouts of exercise (Scholten, Sergeev, Song, & Birger, 2015)

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