



急性高强度间歇运动和中等强度持续运动对2型糖尿病患者餐后血糖、胰岛素和炎症因子的影响

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摘要:目的:对比高强度间歇运动(high intensity interval training, HIIT)和中等强度持续运动(moderate intensity continuous training, MICT)对30~50岁男性2型糖尿病(type 2 diabetes, T2D)患者餐后血糖控制和炎症因子的影响。方法:14位男性T2D受试者[年龄:(42.6±6.5)岁]进行3次交叉随机自身对照试验,每次干预均在早餐后1h进行,分别为:1)HIIT,高强度运动以90% $\dot{V}O_{2max}$ 强度骑功率车7组×1 min/组,低强度运动以30% $\dot{V}O_{2max}$ 强度骑功率车7组×2 min/组,热身以60% $\dot{V}O_{2max}$ 强度骑功率车4 min,恢复以40% $\dot{V}O_{2max}$ 强度骑功率车5 min;2)MICT,以50% $\dot{V}O_{2max}$ 强度持续骑功率车30 min;3)安静对照(CON)在功率车上静坐30 min,每次干预间隔10天。受试者分别在运动前、运动后即刻和运动后1 h 3个时间点抽取静脉血,测试血糖、胰岛素、TNF- α 和IL-6水平,并计算干预后相比干预前的变化量,采用双因素重复测量方差分析对血糖、胰岛素、TNF- α 和IL-6水平及变化进行比较。结果:30 min的HIIT和MICT总能量消耗量无显著差异。相比CON,HIIT和MICT显著降低了运动后即刻血糖水平($P<0.001$),且相比MICT,HIIT使血糖降低更明显($P<0.01$);相比运动后即刻,HIIT使血糖水平在运动后1 h显著回升($P<0.05$),而此时MICT导致血糖降低量仍显著多于CON的降低量($P<0.01$)。相比CON,HIIT和MICT显著降低了胰岛素水平($P<0.01$),但HIIT和MICT二者之间无显著差异;HIIT($P<0.001$)和MICT($P<0.01$)显著增加了运动后即刻TNF- α 水平,但在运动后1 h恢复至运动前水平。不同运动方式对IL-6水平没有产生显著影响($P>0.05$)。结论:急性HIIT和MICT均可以降低30~50岁男性T2D患者餐后静脉血血糖和胰岛素水平,并短暂提高炎症因子TNF- α 的水平;相比MICT,HIIT在运动后即刻的降糖效果更好。

关键词:高强度间歇运动;中等强度持续运动;血糖;胰岛素;TNF- α ;2型糖尿病

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2型糖尿病(type 2 diabetes, T2D)是当前严重危害人类健康的慢性疾病之一。根据2013年全国大样本流行病学调查报告,我国成人糖尿病患病率已达到10.9%,并具有年轻化趋势(Wang et al., 2017)。T2D的防控刻不容缓。

运动被视为预防T2D及其健康管理的有效干预方法(Colberg et al., 2016; Umpierre et al., 2011)。近年来,有关高强度间歇运动(high intensity interval training, HIIT)的研究发现,与传统的中等强度持续有氧运动(moderate intensity continuous training, MICT)相比,HIIT在改善心血管健康(Costa et al., 2018)、骨骼肌重塑(Cui et al., 2019)、血糖调节(Helge et al., 2019; Wormgoor et al., 2018)等方面产生了相似甚至更优的效果。HIIT受到了众多学者的关注。

规律运动对T2D的防治意义重大,急性运动对经常静坐少动的T2D患者的血糖调节也有影响。有研究发现,一次急性MICT可以有效降低T2D患者餐后血糖水平

(Colberg et al., 2010; Larsen et al., 1997; Santiago et al., 2018)。另有研究指出,急性HIIT对于降低餐后血糖的效果更好(Karstoft et al., 2014; Mendes et al., 2019)。此外,有研究强调,血糖的变化程度由运动时的总能量消耗决定,与运动强度无关(Larsen et al., 1999; Terada et al., 2016; Wormgoor et al., 2018)。而急性运动对餐后胰岛素的影响鲜有报道。因此,急性HIIT与MICT对T2D患者餐后血糖

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及胰岛素的影响有待进一步研究。

临床研究发现,慢性低水平的炎症状态促进了T2D的发生发展(Donath et al., 2011; Prattichizzo et al., 2018),而规律运动可以显著抑制血清TNF- α 和IL-6的升高,保护机体免受炎症因子诱导的胰岛素抵抗的影响(陈谨, 2020; 肖全红, 2011; Chen et al., 2020)。此外,有研究发现,急性运动可以降低健康受试者运动后1h的血浆TNF- α 水平(Durrer et al., 2017),但该结果是否适用于T2D患者尚不明了。本研究将对急性HIIT和MICT对30~50岁男性T2D患者餐后血糖和炎症因子水平的影响。

1 研究对象与方法

1.1 研究对象

本研究共招募了18名T2D患者,纳入标准:男性,30~50岁,病程0.5~5年(表1)。排除标准:1)其他类型的糖尿病患者;2)空腹血糖 >11.1 mmol/L, HbA1c $>8.0\%$, BMI >28 或 <18.5 kg/m 2 ;3)存在心血管疾病及风险者;4)肝功能、甲状腺功能、肌酸激酶异常者;5)胰岛素使用者;6)吸烟者;7)各种运动禁忌症患者;8)实验前3个月内参加其他实验者;9)实验前6个月内进行了规律的体育运动者。排除不符合条件的4人后,共14名受试者被纳入本研究。所有人自愿签署《知情同意书》,填写《基本情况问卷调查表》《运动风险筛查(PARQ问卷)》和《运动测试的禁忌症排查表》。本研究通过了伦理委员会审查。

表1 受试者特征

Table 1	Participants' Characteristics	<i>n</i> =14
变量	<i>M</i> \pm <i>SD</i>	区间
年龄/岁	42.6 \pm 6.5	30~50
病程/年	1.8 \pm 1.0	1~4.5
BMI/(kg·m $^{-2}$)	24.5 \pm 2.2	21.1~27.7
空腹血糖/(mmol·L $^{-1}$)	7.0 \pm 1.7	5.1~10.8
空腹胰岛素/(μ U·mL $^{-1}$)	10.3 \pm 4.8	4.9~23.5
HbA1c/%	6.9 \pm 1.0	5.4~8.4
空腹IL-6/(pg·mL $^{-1}$)	4.3 \pm 1.0	3.0~6.4
空腹TNF- α /(pg·mL $^{-1}$)	6.5 \pm 1.4	4.5~9.5
最大摄氧量($\dot{V}O_{2max}$)/(mL·min $^{-1}$ ·kg $^{-1}$)	25.5 \pm 5.1	19.0~32.4
最大功率(P_{max})/W	141.1 \pm 18.6	100~175
最大心率(HR_{max})/bpm	169.1 \pm 10.1	151~188

1.2 研究方法

受试者首先进行基线测试,包括血液、生理和形态指标的检测以及运动负荷试验。10天后,进行HIIT, MICT和安静对照3次交叉随机自身对照试验。每次干预均在早餐后1h进行,每次干预间隔10天。试验的随机化是通过让受试者随机选择并打开不透明的密封信封实现的,每个信封内仅包含一种干预方式。整个研究期间,要求受试者保持原有的生活活动(饮食、用药、身体活动保持不变),在每个干预日当天和干预日前一晚,摄入相同的早餐和晚餐(由

研究人员提供)。干预日前24h内不能饮酒、含咖啡因饮料和剧烈运动。

1.3 测试方法

1.3.1 血液指标测试

基线测试时,受试者进行空腹肘前静脉取血,检测空腹葡萄糖、胰岛素、糖化血红蛋白、游离脂肪酸、TNF- α 和IL-6水平等。在3次随机运动干预实验中,受试者分别在运动前(早餐后1h),运动后即刻(早餐后1.5h)和运动后1h(早餐后2.5h)测试静脉血血糖、胰岛素、TNF- α 和IL-6的水平。所有测试方法均按照说明书进行,其中,血糖测试采用己糖激酶法,糖化血红蛋白采用散射比浊法,胰岛素采用电化学发光法,IL-6和TNF- α 采用化学发光法。所有样品进行双样本复查。

1.3.2 形态指标测试

测试受试者的身高和体重,并计算身体质量指数(body mass index, BMI),即体质量(kg)/身高 2 (m 2)。

1.3.3 运动负荷试验

采用Cortex MetaLyzer 3B气体代谢分析仪和Polar心率遥测仪分别测试最大摄氧量($\dot{V}O_{2max}$)和最大心率(HR_{max}),每30s进行一次数据采集。每次测试前按要求进行系统校准。运动负荷试验以功率自行车为运动方式,起始负荷为0W,之后每2min增加25W,转速为60r/min,直至力竭。 $\dot{V}O_{2max}$ 的判定标准为:1) $HR \geq 100\% HR_{max}$ ($HR_{max} = 220 - \text{年龄}$);2)呼吸交换率(respiratory exchange ratio, RER) >1.10 ;3)受试者已尽最大能力,无法再维持预定转速(Howley et al., 1995; Karstoft et al., 2014; Winding et al., 2018)。同时采用Borg量表(6-20)(Borg, 1982)记录主观疲劳感觉(rate of perceived exertion, RPE)。

1.4 干预方法

所有干预实验在专业人员的监督和指导开展。基于文献研究(Francois et al., 2017; Gillen et al., 2012; Larsen et al., 2019)和本研究的预实验,确定HIIT和MICT的运动方案。HIIT运动方案:以90% $\dot{V}O_{2max}$ 强度运动7组 \times 1min/组,以30% $\dot{V}O_{2max}$ 强度运动7组 \times 2min/组,以60% $\dot{V}O_{2max}$ 强度热身4min,以40% $\dot{V}O_{2max}$ 强度恢复5min。MICT运动方案:以50% $\dot{V}O_{2max}$ 强度持续运动30min。运动干预采用功率自行车的运动方式,蹬踏节奏为60r/min。CON组受试者在功率自行车上静坐30min。采用Cortex MetaLyzer 3B气体代谢分析仪和Polar心率遥测仪获取每30s的气体交换和心率数据,不同干预时30min总能量消耗量(kcal)的计算参考江崇民等(2011)的研究。采血时受试者在功率车上保持静坐状态。

1.5 数据处理与统计

采用SPSS 19.0对数据进行统计分析,数据以平均值 \pm 标准差($M \pm SD$)表示。计算各指标不同时间点相比干预前的变化量(干预后-干预前的安静状态),采用配对

样本 *t* 检验对两种运动的总能量消耗进行比较,采用双因素重复测量方差分析(运动方式×时间)对不同干预方式下不同时间点的血糖、胰岛素、TNF- α 和 IL-6 浓度及变化量进行比较。 $P < 0.05$ 表示组间差异显著。

2 结果

本研究共有 13 名受试者完成全部实验。13 名受试者在进行 HIIT 和 MICT 时均无不良反应,两种运动的总能量消耗量(173.32±21.71 kcal vs 168.87±24.24 kcal)无统计学差异($P > 0.05$),但均显著高于 CON 组($P < 0.001$)。

2.1 不同运动方式下血糖和胰岛素的急性反应

血糖和胰岛素的浓度变化见表 2。对比不同时间下不

同干预方式导致的血糖浓度变化发现,存在运动方式×时间的交互作用($F=6.600, P=0.014$)。运动后即刻,与 CON 组相比,MICT(-2.49±1.76 mmol/L vs 0.32±1.13 mmol/L, $P < 0.001$)和 HIIT(-3.60±1.41 mmol/L vs 0.32±1.13 mmol/L, $P < 0.001$)使血糖浓度明显降低,且相比 MICT,HIIT 使血糖浓度降低地更多($P < 0.01$,图 1A)。运动后 1 h,MICT 使血糖浓度的降低仍明显多于 CON(-2.45±2.12 mmol/L vs -0.51±1.69 mmol/L, $P < 0.01$,图 1A),HIIT 使血糖浓度的降低仅有多于 CON 组的趋势,无统计学差异(-2.38±2.12 mmol/L vs -0.51±1.69 mmol/L, $P=0.061$,图 1A)。同时,相比运动后 1 h,HIIT 使运动后即刻血糖降低地更多($P < 0.05$,图 1A)。

表 2 静脉血糖、胰岛素、TNF- α 和 IL-6 的浓度
Table 2 Glucose, Insulin, TNF- α and IL-6 Levels

	组别	运动前	运动后即刻	运动后 1 h
血糖/(mmol·L ⁻¹)	CON	9.48±2.98	9.80±2.50	8.98±2.99 [#]
	HIIT	9.86±2.16	6.28±2.19 ^{***@###&}	7.49±3.18 ^{##}
	MICT	9.77±2.90	7.27±3.13 ^{**###}	7.32±3.23 ^{##}
胰岛素/(μ U·mL ⁻¹)	CON	42.94±21.70	47.03±23.23	46.83±24.73
	HIIT	50.23±23.87	24.19±9.67 ^{**##}	32.61±20.13 ^{##}
	MICT	45.70±24.38	27.10±13.90 ^{**##}	31.25±17.08 [#]
TNF- α /(pg·mL ⁻¹)	CON	5.33±1.62	5.21±1.54	5.24±1.42
	HIIT	5.77±1.66	7.03±1.66 ^{***###&&&}	5.58±1.36
	MICT	5.32±1.68	6.43±1.54 ^{**###&&&}	4.98±1.62
IL-6/(pg·mL ⁻¹)	CON	4.11±1.52	4.22±1.54	4.20±1.80
	HIIT	3.79±0.90	4.35±0.82	4.17±1.32
	MICT	3.92±1.27	3.90±1.01	4.11±1.93

注:与 CON 相比,*表示 $P < 0.05$,**表示 $P < 0.01$,***表示 $P < 0.001$;与 MICT 相比,@表示 $P < 0.05$;与干预前相比,#表示 $P < 0.05$,##表示 $P < 0.01$,###表示 $P < 0.001$;与干预后 1 h 相比,&表示 $P < 0.05$,&&&表示 $P < 0.001$ 。

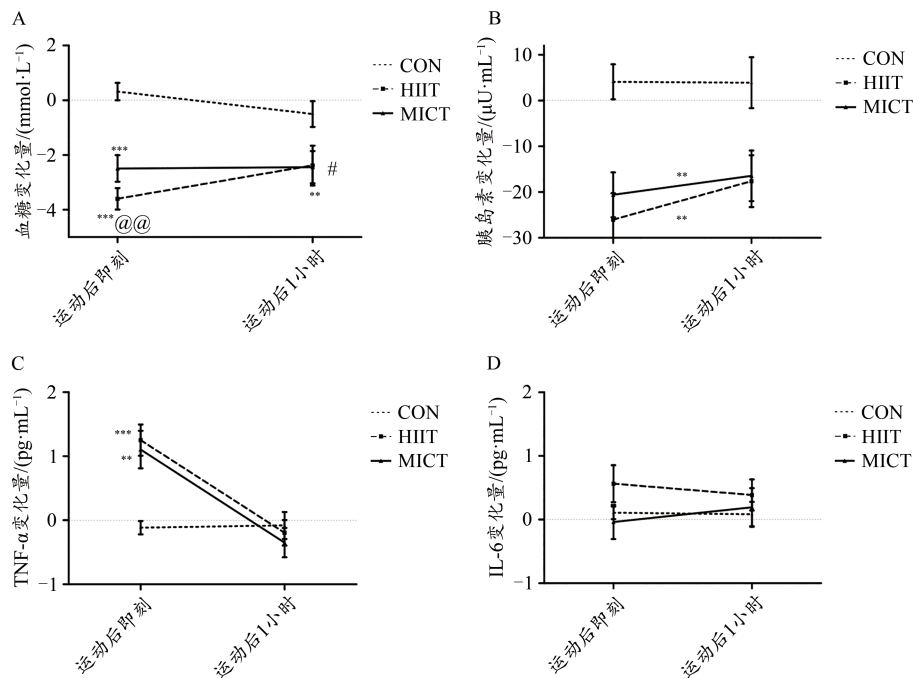


图 1 不同运动方式下静脉血糖(A)、胰岛素(B)、TNF- α (C)和 IL-6(D)的变化

Figure 1. The Changes of Glucose (A), Insulin (B), TNF- α (C) and IL-6 (D) under Different Interventions

注:与 CON 相比,**表示 $P < 0.01$,***表示 $P < 0.001$;与 MICT 相比,@@表示 $P < 0.01$;与运动前相比,#表示 $P < 0.05$ 。

胰岛素的变化存在干预方式主效应($F=8.576, P=0.007$)。与CON组相比,HIIT组($P<0.01$)和MICT组($P<0.01$)的胰岛素降低量显著增加,但HIIT和MICT之间无显著差异($P>0.05$)。

2.2 不同运动方式下TNF- α 和IL-6的急性反应

TNF- α 和IL-6的变化情况见表2。对比不同时间下不同干预方式导致的TNF- α 浓度变化发现,存在运动方式 \times 时间的交互作用($F=16.675, P<0.001$)。运动后即刻,与CON组相比,MICT(1.10 ± 1.06 pg/mL vs -0.12 ± 0.37 pg/mL, $P<0.01$)和HIIT(1.28 ± 0.82 pg/mL vs -0.12 ± 0.37 pg/mL, $P<0.001$)使TNF- α 浓度明显提高,且HIIT($P<0.001$)和MICT($P<0.01$)在运动后即刻的TNF- α 浓度均比运动前显著增加(图1C)。在运动后1h,相比运动后即刻,两种运动方式使TNF- α 浓度显著下降($P<0.001$),但此时两种运动方式与CON之间的TNF- α 浓度变化量无显著差异($P>0.05$,图1C)。

不同时间下不同运动对IL-6浓度的变化没有产生明显的影响($P>0.05$,图1D)。

3 分析与讨论

3.1 急性HIIT和MICT对血糖、胰岛素水平的影响

以往的研究(Larsen et al., 1997, 1999; Gillen et al., 2012)发现,急性运动可有效减轻T2D患者的餐后高血糖和高胰岛素血症症状。本研究也同样观测到餐后HIIT和MICT使T2D患者的血糖、胰岛素水平显著下降。研究发现,运动后即刻,HIIT产生的降糖效应明显大于MICT,体现出HIIT这种高-低强度的间歇运动的降糖优势,但该优势并未在运动后的恢复期持续下去,即运动后1h,HIIT组血糖浓度相对运动后即刻有所回升,这对于避免低血糖的发生有一定意义。在运动后的恢复期,两种运动的血糖降低量均大于CON组,使血糖保持在较低水平。

胰岛素是机体唯一的降糖激素,而T2D患者却遭受胰岛素抵抗和胰岛素分泌不足的影响(Stumvoll et al., 2005)。本研究发现,HIIT和MICT引起了胰岛素水平的下降,与以往的研究相一致(Larsen et al., 1997),推测这与血糖浓度降低和交感神经活动增加有一定关系。本研究未观测到两种急性运动对胰岛素水平影响的差异,因而高强度间歇的运动方式可能不是影响T2D患者胰岛素变化的决定性因素。

3.2 急性HIIT和MICT对TNF- α 和IL-6的影响

研究发现,TNF- α 是外周胰岛素抵抗的关键分子(Pedersen, 2017; Plomgaard et al., 2005),可以直接损害外周胰岛素刺激的葡萄糖摄取,破坏糖稳态,而规律运动可以降低炎症因子(C反应蛋白、IL-6、TNF- α)的水平,缓解T2D患者的慢性炎症状态(Chen et al., 2020; De Lemos et

al., 2012)。本研究发现,单次、急性HIIT和MICT使TNF- α 出现先增高后降低的波动,TNF- α 水平在运动后1h恢复至运动前水平。但Durrer(2017)等的研究发现,急性HIIT并没有使TNF- α 浓度明显提高,只是使TNF- α 浓度在运动后1h显著降低。造成这种不一致的原因可能与受试者的年龄(45岁中青年vs 57岁中老年)、性别(男性vs 男性+女性)、BMI水平(超重vs 肥胖)及运动经历(无vs 有)有关。此外,在本研究中,TNF- α 浓度的波动范围为 5.21 ± 1.54 pg/mL $\sim 7.03\pm 1.66$ pg/mL,远低于其他学者(张华等, 2015)对我国T2D患者TNF- α 水平(26.52 ± 8.57 pg/mL)的报道,该研究对象为中老年T2D患者,而本研究对象为中青年T2D患者,且无并发症。推测T2D患者血清TNF- α 水平可能与年龄和疾病状态(是否有T2D并发症)有关。本研究中HIIT和MICT急性运动后即刻TNF- α 增加,很可能是由于机体产生了较高水平的应激反应,而急性运动诱导的炎症应答反应是机体最重要的防御机制之一。但是,TNF- α 水平的增高并没有持续,在运动后1h TNF- α 水平恢复至干预前,并未产生持续的炎症反应,这对于机体也是种保护效应。此外,研究发现,长期规律运动可以降低T2D患者的炎症反应和氧化应激(Chen et al., 2020),使机体产生良好的适应,可见T2D患者长期规律运动的必要性。

研究发现,急性运动可以通过增加IL-6来抑制TNF- α 的增加,并改善外周胰岛素敏感性(Pedersen, 2017)。此外,运动时间越长,IL-6的反应程度越明显。而本研究对象是T2D患者,数据显示,HIIT和MICT急性运动并没有使IL-6明显改变,TNF- α 也并未受到抑制,这可能是由于本研究的运动时间(30 min)不足以引起IL-6浓度的改变。

上述结果提示,运动诱导的TNF- α 和IL-6的改变不依赖于持续或者间歇的运动方式。运动诱导餐后血糖改善和炎症因子反应的分子机制有待进一步探索(Li et al., 2019)。虽然相比MICT,HIIT在运动后即刻具有更好的降糖效果,但二者对T2D患者餐后胰岛素和TNF- α 的影响效果相似,因此T2D患者可以根据个人喜好和意愿,进行HIIT或者MICT的选择。HIIT最好在专业人士的指导和监督下练习,并准备积极的运动风险防范措施。

4 结论

急性HIIT和MICT均可以降低30~50岁男性T2D患者餐后静脉血血糖和胰岛素水平,并短暂提高炎症因子TNF- α 的水平;相比MICT,HIIT在运动后即刻具有更好的降糖效果。

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The Association of the Body Mass Index of Children with 24-Hour Activity Composition and Isotemporal Substitution: A Compositional Data Analysis

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Abstract: Objective: To examine the relationships between 24-hour activity behaviors and body mass index (BMI) in Shanghai children by using compositional analyses. Methods: A cross sectional study was conducted on 321 primary school students (158 boys and 163 girls) aged 6–13 years in Shanghai. Time spent in 24-hour activity behaviors was determined by accelerometry, children's height and weight were measured by standard instruments. Compositional linear regression models were used to synthetically analyze the associations between the distribution of time spent 24-hour activity behaviors and zBMI, and the effect of compositional isotemporal substitution of 24-hour activity behaviors with zBMI was investigated as well. Results: 1) By controlling for gender and age, time spent in moderate-to-vigorous physical activity (MVPA) ($\beta=-0.75$, $P<0.001$) and light physical activity (LPA) ($\beta=-0.13$, $P<0.05$) was negatively associated with zBMI in children, while the time spent in sedentary behavior ($\beta=0.61$, $P<0.001$) and sleep ($\beta=0.53$, $P<0.01$) was positively correlated with zBMI; 2) The compositional isotemporal substitution models revealed reductions in zBMI when a 15-min reallocation from LPA, sedentary behavior and sleep to MVPA, and from sedentary behavior to LPA; however, a 15-min reallocation from MVPA to LPA, sedentary behavior and sleep, and from LPA to sedentary behavior was associated with higher zBMI; 3) According to the "dose-response" curves, firstly, the mutual substitution of MVPA and other activities has an asymmetric effect on zBMI and the substitution of LPA and sedentary behavior has a symmetrical effect on zBMI; secondly, the best reduction effect on zBMI is to replace sedentary behavior with MVPA; thirdly, with the increase time of MVPA isotemporal substitute other behaviors, the decrease in zBMI was slowed down, otherwise it increased rapidly. Conclusions: Parents and teachers should take 24-hour activities as a whole and attach great importance to the positive effects of MVPA and LPA, try to reallocate time from ST to MVPA and LPA of children so as to obtain better health benefits.

Keywords: physical activity; sedentary behavior; sleep; body mass index; compositional data analysis; isotemporal substitution

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Acute Effects of High-Intensity Interval Training and Moderate-Intensity Continuous Training on Plasma Glucose, Insulin and Inflammatory Factors Levels in Type 2 Diabetic Men

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Abstract: Objective: To compare the acute effects of highintensity interval training (HIIT) versus moderateintensity continuous training (MICT) on postprandial plasma glucose control and inflammatory factors in type 2 diabetic (T2D) men aged 30-50 years. Methods: 14 T2D men (42.6 ± 6.5 years old) underwent a randomized three crossover trial. The three interventions are as follows: HIIT, 7×1 min at 90% maximal oxygen uptake ($\dot{V}O_{2max}$) + 7×2 min at 30% $\dot{V}O_{2max}$ + 4 min warming up at 60% $\dot{V}O_{2max}$ + 5 min cooling at 40% $\dot{V}O_{2max}$ with cycling; MICT, 30 min at 50% $\dot{V}O_{2max}$ with cycling, and a sedentary control (CON) in the postprandial state. Each intervention had a 10 days wash-out period. Plasma glucose, insulin, TNF- α and IL-6 levels were measured at pre-exercise, post-exercise and 1 h post-exercise. Two-way ANOVA with repeated measures were used to compare glucose, insulin, TNF- α and IL-6 values among the interventions. Results: Total energy expenditure between the two exercises was not significantly different. Lower plasma glucose levels were observed immediately after exercise in HIIT and MICT than that of CON ($P<0.001$), the glucose level in HIIT was also lower than that of MICT ($P<0.01$). Glucose levels in HIIT group was increased at 1 h post-exercise compared to immediately post-exercise ($P<0.05$), while the decrease (1 h post-exercise minus pre-exercise) of MICT group was more than that of CON group ($P<0.01$). HIIT and MICT ($P<0.01$) decreased the insulin levels compared to CON, while no difference was observed between the HIIT and MICT. HIIT ($P<0.001$) and MICT ($P<0.01$) increased the TNF- α levels at immediately after exercise but returned to the levels of pre-exercise at 1 h post-exercise. Different exercise types have no obvious effect on IL-6. Conclusion: Both acute HIIT and the matched MICT can lower postprandial plasma glucose and insulin levels in type 2 diabetic men aged 30-50 years, and temporarily increase the level of TNF- α . Compared with MICT, HIIT decreases glucose level greater at immediately post-exercise.

Keywords: highintensity intermittent exercise; moderateintensity continuous exercise; glucose, insulin, TNF- α ; type 2 diabetes