ORIGINAL ARTICLE

Decreased maximal aerobic capacity with use of a triphasic oral contraceptive in highly active women: a randomised controlled trial

C M Lebrun, M A Petit, D C McKenzie, J E Taunton, J C Prior

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Background: Oral contraceptives are commonly used by women athletes. However, their effect on athletic performance is unclear.

Objectives: To examine the effects of a moderate dose, triphasic oral contraceptive on measures of athletic performance in highly trained women athletes.

Methods: This is a double blind, placebo controlled trial in 14 women with ovulatory menstrual cycles and maximal aerobic capacity ($\text{VO}_{2\text{MAX}}$) ≥ 50 ml/kg/min. Four measures of athletic performance were tested: $\text{VO}_{2\text{MAX}}$, anaerobic capacity (anaerobic speed test), aerobic endurance (time to fatigue at 90% of $\text{VO}_{2\text{MAX}}$), and isokinetic strength (Cybex II dynamometer). Height, weight, and six skinfold measurements were also recorded. All these observational tests were completed during both the follicular and mid-luteal phases of an ovulatory menstrual cycle. Cycle phases were confirmed by assaying plasma oestradiol and progesterone. Participants were subsequently randomly assigned to either a triphasic oral contraceptive or placebo and retested in identical fashion (oral contraceptive phase).

Results: Absolute and relative changes in $\text{VO}_{2\text{MAX}}$ from follicular to oral contraceptive phase decreased in the oral contraceptive group by 4.7%, whereas the placebo group showed a slight increase (+1.5%) over the same time period. Two of the women taking oral contraceptive had decreases of 4 and 9 ml/kg/min. In contrast, most women in the placebo group improved or maintained $\text{VO}_{2\text{MAX}}$. There was also a significant increase in the sum of skinfolds in women taking oral contraceptive compared with those taking placebo ($p < 0.01$). There were no significant changes in other physiological variables (maximum ventilation, heart rate, respiratory exchange ratio, packed cell volume) or measures of performance (anaerobic speed test, aerobic endurance, isokinetic strength) as a function of oral contraceptive treatment.

Conclusions: The decrease in $\text{VO}_{2\text{MAX}}$ that occurs when oral contraceptive is taken may influence elite sporting performance in some women. Further studies are required to determine the mechanisms of this change.

See end of article for authors' affiliations

Correspondence to:
Dr Lebrun, Fowler Kennedy
Sport Medicine Clinic 3M
Centre, University of
Western Ontario, London,
ON, Canada N6A 3K7;
clebrun@uwo.ca

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Elite women athletes are prescribed oral contraceptives for a variety of purposes, including contraception, cycle regulation, control of dysmenorrhoea, and treatment of amenorrhoea. Compared with the first generation pills, newer, moderate dose, triphasic formulations have fewer side effects such as weight gain, fluid retention, and alterations in lipid profiles.^{1,2} However, even these moderate dose oral contraceptive formulations have ethinyl oestradiol levels that are 3–5 times the oestrogen equivalent of endogenous oestradiol, and norethindrone levels that are 1–2 times (spread over 21 days) higher progestin levels than endogenous progesterone.³ The effects of these high levels of exogenous hormones on muscle strength, aerobic capacity, and athletic performance are not known.

A few controlled trials have examined effects of oral contraceptive on indicators of exercise performance. A wide diversity in the oestrogen and progestin components of the oral contraceptive, the range of fitness parameters assessed, and varying fitness levels of the participants make the studies difficult to interpret. Results were mixed, showing changes in substrate metabolism, improved running economy,⁴ decreased $\text{VO}_{2\text{MAX}}$ ^{5,6} in conjunction with a significant reduction in mitochondrial citrate, or no significant effects of oral contraceptive on performance.^{7–9} Overall, there is a lack of consensus about the effects of oral contraceptives on athletic performance.^{10,11} To our knowledge, there are no randomised studies of the effects of oral contraceptive on performance in highly trained athletes.

We previously reported observational changes in aerobic performance across the menstrual cycle in 16 highly trained female athletes.¹² As an extension of that study, the same women were subsequently randomised to oral contraceptive or placebo for two months, and retested between days 14 and 17 of the second cycle. The purpose of this randomised double blind, placebo controlled study was to examine characteristics of athletic performance with oral contraceptive use in highly active women.

METHODS AND MATERIALS

Subjects

Ethical approval was obtained from the committee on human experimentation of the University of British Columbia, and all participants gave written informed consent. Athletic women aged 18–40 were recruited. Women were initially excluded if they did not meet the following criteria: (a) regular menstrual cycles (24–35 days in length); (b) no oral contraceptive use in the three months before entering the study; (c) participating on a regular basis in competitive aerobic activity—that is, running, cycling, triathlon, rowing, cross country skiing.

At an initial screening session, $\text{VO}_{2\text{MAX}}$ and general health history were assessed. Volunteers who had $\text{VO}_{2\text{MAX}}$ values less than 50 ml/kg/min were excluded. Women were further excluded if they had any potential risk factors for oral contraceptive administration including smoking, any significant past medical condition, or were taking any medication that

Figure 1 Study design showing three cycles with testing twice in the first cycle and once during the second treatment cycle. OC, Oral contraceptive; MSSE, Medicine and Science in Sports and Exercise.¹²

might interfere with exercise testing or administration of oral contraceptive. Participants were also required to have a physical examination, including a pelvic examination and Pap smear, carried out by their own doctor. Women taking supplements or iron were asked to maintain the exact dosage throughout the entire length of the three cycle study (of which this controlled trial was the third cycle).

Of the 51 volunteers for the initial study,¹² 17 met all criteria and completed all three tests (follicular, luteal, and oral contraceptive or placebo). Three of these 17 women did not show hormonal evidence of ovulation during the observational study, and their test results were subsequently excluded from the analyses. Data are presented for 14 women who completed this controlled trial.

Study design

Figure 1 presents an overview of the study design and testing protocol. Testing was performed during both the early follicular (days 3–8) and mid-luteal (days 4–9 after “ovulation”) phases of an ovulatory menstrual cycle. A resting level of serum progesterone higher than 16 nmol/l was required to confirm ovulation.¹³ After follicular and luteal phase tests, participants were randomly assigned to either an oral contraceptive ($n = 7$) or placebo ($n = 7$) group. Participants and investigators were blind to group assignment.

A triphasic oral contraceptive (Synphasic; Pharmacia Canada, Mississauga, Ontario, Canada) was used. Synphasic contains a constant concentration of 0.035 mg ethinyl oestradiol and two different doses of norethindrone in three phases (days 1–7, 0.5 mg; days 8–16, 1.0 mg; and days 17–21, 0.5 mg) equalling a total norethindrone dose of 15.0 mg over the 21 day cycle. All women took an unmarked lactose capsule containing either oral contraceptive or placebo following the recommended schedule of daily administration for three consecutive weeks and stopping for one week. Capsules were taken as above for two consecutive months. The treatment testing session was performed between days 14 and 17 (mean (SD) 14.4 (0.5) days) of the second cycle of oral contraceptive or placebo administration (fig 1). These days were chosen as these were the last days of the highest progestin dose of the triphasic oral contraceptive.

Testing protocol

All tests were completed on two successive days during each phase (follicular, luteal, and treatment). Because of the double blind nature of the study, treatment phase tests were conducted on days 14–17 of the cycle rather than based on day of ovulation. Although this may theoretically be during the luteal phase in the subjects on placebo, there was a high degree of individual variability in the actual day of ovulation. Most women were actually in the mid- or late-follicular phase according to serum progesterone levels. Two women in each group appeared to have ovulated before oral contraceptive treatment tests.

For the first day, participants reported to the laboratory in a fasted, resting state, and venous blood samples, $\text{VO}_{2\text{MAX}}$, and anaerobic performance were assessed. Measurements of isokinetic strength, aerobic endurance, and assessment of body composition were completed on the second day of testing.

Anthropometry and body composition

Height and weight (Detecto industrial scale) were measured to the nearest 0.1 cm and 0.1 kg respectively. Skinfold thickness was measured at six sites (biceps, triceps, subscapular, suprailiac, anterior thigh, and medial calf) with a Harpenden skinfold caliper (John Bull, UK British Indicators Ltd, St Albans, Herts, UK). Skinfold measurements are reported as the sum of all values. Percentage body fat was assessed by underwater densitometry and calculated using the Siri formula.¹⁴

Blood samples

Blood samples (15 ml) were obtained by venepuncture. They were kept cool (in an ice/water bath), and processed when testing was completed. One tube was taken to the laboratory at the University Hospital for determination of an automated blood count (Coulter S + STKR). The remaining blood was spun in a refrigerated centrifuge (Damon/IEC Clini-Cool) for 10 minutes at 3000 rpm. Plasma was stored in Venoject plain silicone coated glass tubes at -20°C until analysis using commercially available no extraction, solid phase ¹²⁵I radioimmunoassays (Coat-A-Count Estradiol and Coat-A-Count Progesterone; Diagnostic Products Corporation). Over the duration of the study, blood samples were coded and analysed in three separate batches by an independent observer. All samples from one woman were analysed together, and at least one participant from each of the two experimental groups was included in each assay. Intra-assay coefficients of variation were 10.6% for oestradiol and 10.3% for progesterone. Interassay coefficients of variation ranged from 4.2 to 8.1% for oestradiol and from 7.2 to 10.0% for progesterone (Diagnostic Products Corporation, Los Angeles, California, USA). Assay sensitivities were 2.9 pmol/l for oestradiol and 0.16 nmol/l for progesterone. The oestradiol assay does not detect the ethinyl oestradiol and the progesterone assay does not detect the norethindrone in this oral contraceptive.

Aerobic capacity

$\text{VO}_{2\text{MAX}}$ was assessed using a standard running protocol.¹⁵ After a 10 minute warm up at a self selected pace (between 2.2 and 2.7 m/s), a continuous progressive workload was carried out on a level grade, beginning at a speed of 2.2 m/s, and increasing by 0.22 m/s each minute until fatigue. Heart rate was monitored using a Polar Vantage heart rate monitor and recorded at 45 seconds into each stage. Expired gases were continuously sampled and analysed using a Beckman Metabolic Measurement Cart (OM-11 oxygen analyser and

	Oral contraceptive group			Placebo		
	Follicular	Luteal	Treatment	Follicular	Luteal	Treatment
Weight (kg)	60.2 (54.3 to 66.2)	60.6 (54.5 to 66.8)	61.2 (55.0 to 67.5)	59.9 (54.0 to 65.8)	59.9 (53.7 to 66.0)	59.8 (53.5 to 66.0)
Body fat (%)	16.5 (12.7 to 20.4)	16.9 (13.9 to 20.0)	17.5 (13.7 to 21.3)	17.4 (13.5 to 21.3)	17.1 (14.0 to 20.1)	16.9 (13.0 to 20.7)
Sum of skinfolds (mm)	68.8 (55.7 to 81.9)	73.1 (59.9 to 86.4)	79.2 (63.6 to 94.8)	80.1 (67.0 to 93.2)	78.9 (65.7 to 92.2)	76.3 (60.7 to 92.0)**
Oestradiol (pmol/l)	138.7 (88.4 to 189.0)	442.1 (324.6 to 559.6)	347.6 (136.4 to 558.7)	133.7 (83.4 to 184.0)	412.6 (295.1 to 530.1)	364.4 (153.3 to 575.6)*
Progesterone (nmol/l)	3.3 (1.0 to 1.6)	40.1 (26.9 to 53.4)	24.7 (4.3 to 45.1)	1.1 (0.8 to 1.4)	44.2 (31.0 to 57.5)	19.5 (1.0 to 39.9)*
Haemoglobin (g/l)	131.3 (126.7 to 135.9)	132.6 (128.6 to 136.5)	130.7 (126.9 to 134.5)	133.1 (128.6 to 137.7)	134.4 (130.5 to 138.4)	135.7 (131.9 to 139.5)
Packed cell volume (%)	38.5 (37.3 to 39.7)	39.2 (38.3 to 40.2)	38.7 (37.5 to 39.9)	39.0 (37.7 to 40.2)	39.3 (38.4 to 40.3)	39.9 (38.7 to 41.1)
Mean cell volume (fl)	91.9 (89.0 to 94.7)	92.3 (89.1 to 95.5)	91.8 (88.6 to 95.1)	92.0 (89.1 to 94.9)	91.7 (88.6 to 94.9)	92.9 (89.6 to 96.1)
VO ₂ MAX (litres/min)	3.29 (3.00 to 3.59)	3.26 (3.00 to 3.52)	3.18 (2.94 to 3.43)	3.16 (2.86 to 3.45)	3.08 (2.82 to 3.34)	3.18 (2.94 to 3.43)**
VO ₂ MAX (ml/kg/min)	54.7 (51.6 to 57.9)	53.7 (51.0 to 56.5)	52.0 (49.0 to 55.1)	53.0 (49.9 to 56.1)	52.0 (49.1 to 54.7)	53.8 (50.7 to 56.8)**
VE (litres/min; BTPS)	104.5 (96.6 to 112.4)	105.3 (97.3 to 113.2)	102.6 (93.7 to 111.4)	108.3 (100.4 to 116.2)	109.3 (101.3 to 117.2)	107.6 (98.8 to 116.5)
Maximal heart rate (bpm)	190.7 (181.8 to 199.7)	190.0 (180.7 to 199.3)	192.6 (181.9 to 203.3)	188.9 (179.9 to 197.8)	188.3 (179.0 to 197.5)	191.0 (180.3 to 201.7)
RER	1.17 (1.12 to 1.21)	1.18 (1.12 to 1.23)	1.16 (1.11 to 1.20)	1.19 (1.14 to 1.23)	1.17 (1.11 to 1.22)	1.12 (1.08 to 1.17)
AST (seconds)	33.0 (26.2 to 39.8)	33.0 (26.4 to 39.6)	32.9 (26.1 to 39.6)	26.1 (19.4 to 32.9)	24.9 (18.3 to 31.4)	26.6 (19.8 to 33.3)
Quadriceps peak torque (N.m)	158.1 (136.9 to 179.4)	153.1 (135.4 to 170.7)	145.1 (123.6 to 166.6)	142.6 (121.4 to 163.9)	141.6 (124.0 to 159.3)	139.2 (117.7 to 160.7)
Hamstrings peak torque (N.m)	89.2 (72.0 to 106.4)	93.4 (79.5 to 107.3)	89.4 (75.6 to 103.2)	76.6 (59.5 to 93.8)	78.9 (65.0 to 92.8)	77.3 (63.5 to 91.1)

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Figure 2 Percentage change in sum of skinfolds from follicular to treatment phase for women in the placebo and oral contraceptive groups.

Figure 3 Percentage change in VO_{2MAX} from follicular to treatment phase for women in the placebo and oral contraceptive groups.

RESULTS

Table 1 presents characteristics for each group in the three phases: follicular phase, luteal phase, and oral contraceptive treatment period. Follicular phase values were not affected by random assignment to oral contraceptive or placebo.

Body composition

Body weight and percentage fat by underwater weighing were similar in the two groups at each phase. Subjects in the oral contraceptive group increased weight (+1 kg) and percentage fat by underwater weighing (+1%) from the follicular to the treatment phase, but those in the placebo group showed no change. Group differences were not significant (group $\times$ phase, $p > 0.05$). Change in sum of skinfolds was significantly different between the groups over time, with a larger increase in the oral contraceptive group (group $\times$ phase, $p = 0.004$; fig 2).

Hormones and blood samples

As expected, oestradiol ($p < 0.01$) and progesterone ($p < 0.01$) values differed significantly between the follicular, luteal, and treatment tests for all subjects, but did not vary as a function of oral contraceptive treatment (table 1). Haemoglobin concentration, packed cell volume, and mean red cell volume did not differ significantly between groups or within each group over time.

Exercise performance

Aerobic capacity

Both absolute and relative VO_{2MAX} differed between the oral contraceptive and placebo groups over time ($p = 0.050$ and $p = 0.019$ respectively). Aerobic capacity decreased in the oral contraceptive group across the three phases. In contrast, there was a slight decrease in VO_{2MAX} between the follicular and luteal phase tests, but an increase in the third test in the placebo group. The mean decrease from the follicular to treatment phase was 4.7% in the oral contraceptive group compared with a 1.5% improvement with placebo. Figure 3 illustrates individual changes. There were no significant fluctuations in maximum minute ventilation ($\dot{V}_E$), maximum

heart rate, or maximum respiratory exchange ratio accompanying changes in VO_{2MAX} .

Endurance performance, anaerobic capacity, and strength

There were no significant differences in endurance performance (at 90% of VO_{2MAX}), anaerobic capacity (as measured by the AST), or isokinetic strength (on a Cybex II dynamometer) within or between groups over time (table 1).

DISCUSSION

To our knowledge, this is the first randomised, double blind, placebo controlled trial of the effects of oral contraceptive on indicators of athletic performance in highly trained women ($VO_{2MAX} = 50$ ml/kg/min). Use of moderate dose triphasic oral contraceptive resulted in a mean decrease in VO_{2MAX} of 4.7% in trained women compared with a 1.5% improvement with placebo. Although there was high individual variability in response to oral contraceptive administration, there was a clear trend towards a detriment in VO_{2MAX} in highly trained women taking oral contraceptive. The decrease in VO_{2MAX} was accompanied by an increase in sum of skinfolds, but not by significant changes in weight or measures of strength, anaerobic, or endurance performance.

Previous studies on the role of oral contraceptive on athletic performance have assessed a variety of performance indicators with varying protocols, duration and type of oral contraceptive use, and fitness levels of participants.^{10–11} Researchers have examined the effect of oral contraceptive on VO_{2MAX} , submaximal endurance performance, strength, anaerobic capacity, and side effects such as weight gain.

Maximal aerobic capacity

Studies in untrained or moderately trained women have shown mixed effects of oral contraceptive use on VO_{2MAX} . Daggett and colleagues⁵ showed a significant reduction in VO_{2MAX} (from 44.6 to 39.8 ml/kg/min) in a group of seven moderately trained women after one to two months of oral contraceptive use. Another study⁶ used a design similar to the present investigation, with both a control group ($n = 6$) and an oral contraceptive group ($n = 6$). Over six months, the control group increased aerobic capacity by about 8% (from 42.6 (2.8) to 45.9 (5.8) ml/kg/min), whereas after six months of monophasic oral contraceptive administration, VO_{2MAX} had decreased by about 7% (from 41.2 (11.8) to 38.4 (9.8) ml/kg/min). Changes were associated with a decrease in the oxygen pulse (12.1 (3.2) to 11.2 (2.2) ml per beat) and were reversible on discontinuation of treatment.⁶ The smaller differences in change in VO_{2MAX} in our study could be due to lower doses of exogenous steroids in the oral contraceptive, shorter duration of administration, or the greater fitness level of our participants. In contrast, other studies showed no effect of oral contraceptives on VO_{2MAX} in moderately trained women.¹⁸

As in our study, the observed decreases in VO_{2MAX} have not been directly linked to significant alterations in O_2 carrying capacity of the blood (haemoglobin concentration or packed cell volume), or other physiological measurements influencing O_2 uptake or delivery to the tissue. Although the mechanisms are unclear, exogenous oestrogen may exert a deleterious effect on aerobic capacity. The changes are probably not due to progestin. A well controlled, randomised, double blind, placebo controlled trial showed that high doses of medroxyprogesterone (20 mg three times/day for five doses) in men had no effect on VO_{2MAX} , but did increase minute ventilation as expected.¹⁹

Submaximal endurance performance

Oral contraceptives have been shown to alter substrate metabolism, including carbohydrates and lipids,^{20–21} and to cause a decrease in blood glucose with heavy exercise.²¹ These

actions, which may be linked to high oestrogen,²² could decrease endurance performance by reducing the fuel available for exercise. In our study, there were no significant differences between oral contraceptive and placebo groups in their performance on the endurance run. In contrast, a recent study reported improved submaximal running economy with oral contraceptive use.⁴ These differences may be partially explained by the type of tests used to assess endurance performance. In our study, participants ran at 90% of $\dot{V}O_{2\text{MAX}}$ until fatigue. Giacomoni and colleagues⁴ assessed running economy at 7, 8, and 9 km/h, equal to about 60–80% $\dot{V}O_{2\text{MAX}}$. In that study, differences in running economy tended to be greater at lower intensities (7 and 8 km/h v 9 km/h). There may be a different response to oral contraceptive use at lower compared with higher intensities of exercise.

Strength and anaerobic capacity

It has been postulated that oral contraceptive use may prevent normal decreases in strength that occur during the luteal phase of a menstrual cycle.²³ We saw no significant differences in measurements of muscle strength with oral contraceptive use or placebo. The overall effect of oral contraceptive on strength remains unknown.

We also saw no changes in anaerobic performance as a function of oral contraceptive use. Although few studies have been performed, there does not appear to be any effect of oral contraceptive on energy metabolism for short term anaerobic work. However, the scores for this test were relatively low in most of the athletes in our study, indicating a low anaerobic capacity. This is consistent with the fact that these subjects were well trained for predominantly aerobic-type activities. The effect of oral contraceptive use on anaerobic performance in highly trained anaerobic athletes should be explored.

Benefits and side effects of oral contraceptives

Potential benefits of oral contraceptive for athletic performance include decreased dysmenorrhoea, iron deficiency, and anaemia risks in women experiencing heavy flow. All participants had normal haemoglobin levels, and there were no significant oral contraceptive related changes in either haemoglobin or packed cell volume over six weeks. This is in agreement with other short term studies.^{6, 24}

Early studies of high dose oral contraceptive formulations documented side effects, including fluid retention and weight gain. Biphasic and triphasic pills contain 30–40% lower levels of hormone and appear to have a corresponding decrease in adverse effects.^{25, 26} In this study, athletes taking oral contraceptive had a non-significant weight gain of about 1 kg over six weeks compared with women in the placebo group. The significant increase in sum of skinfolds in the oral contraceptive group suggests that the weight increase was due primarily to an increase in subcutaneous body fat, although increased water retention cannot be excluded. Overall, recent non-controlled studies suggest no long term change in weight with oral contraceptive use,²⁶ but changes in body composition have not been assessed.

Limitations

A caveat in this type of research (that only became evident during the course of the study) is the relative impossibility of carrying out true double blind studies with oral contraceptives. Approximately half of the participants were aware that they were taking oral contraceptives because of subtle changes, alterations in the pattern of their normal menstrual cycles, and the presence of side effects such as breakthrough bleeding throughout the cycle. Also, as noted, two of the seven women on the moderate dose oral contraceptive actually still showed hormonal evidence of ovulation.

Studies of this nature are also difficult to control because of the tremendous individual variability in timing of ovulation,

Take home message

This randomised, double blind, placebo controlled study showed that oral contraceptive use may decrease aerobic capacity in some highly trained athletes, but there is high individual variability. Further study is needed to determine mechanisms of change and to document whether changes are reversible or persist with longer term use.

response to oral contraceptive treatment, and cycle phase. Although we meticulously performed all treatment phase tests on days 14–17 of the menstrual cycle, there was a high degree of individual variability in the actual day of ovulation in the test cycle. Most women were actually in the mid- or late-follicular phase according to serum progesterone levels. However, two women in each group appeared to have ovulated before treatment tests. Results of our study were similar regardless of the phase with which data were compared. Nonetheless, the difficulty of repeating tests in the exact phase of the cycle over time should be noted.

Summary

The results of this study indicate that administration of this moderate dose triphasic oral contraceptive for two cycles does not have any apparent or measurable effect on most components of athletic performance in this group of elite women athletes. The small decreases in $\dot{V}O_{2\text{MAX}}$ that occurred in women taking oral contraceptive suggest that exogenous oestrogen may exert a deleterious effect on aerobic capacity with potential implications for elite performance. The magnitude of this effect varied between individuals. Further studies are necessary to delineate potential mechanisms of the change in functional aerobic capacity and body weight, and to further document whether changes in performance are reversible on discontinuation of treatment. Studies of the effects of oral contraceptive after longer term use (more than six months), and with larger sample size will also provide important insight into the effects of oral contraceptives on athletic performance. In addition, different formulations of oral contraceptive should be compared.

AUTHORS' NOTE

Since acceptance of our paper, we have learned that another group of authors has published similar findings from their work: Casazza GA, Suh S-H, Miller BF, *et al.* Effects of oral contraceptives on peak capacity. *J Appl Physiol* 2002;**93**:1698–1702

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Authors' affiliations

C M Lebrun, M A Petit, D C McKenzie, J E Taunton, J C Prior, Fowler Kennedy Sport Medicine Clinic 3M Centre, University of Western Ontario, London, ON N6A 3K7, Canada

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