Roux-en-Y gastric bypass surgery converts two alcoholic drinks to four

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Roux-en-Y gastric bypass (RYGB) is the most common bariatric surgical procedure performed in the world[1]. Although RYGB causes a marked reduction in food intake and induces remission of food addiction[2], RYGB is associated with an increased risk of developing alcohol use disorders (AUD) [3]. It is likely that RYGB-related changes in gastro-intestinal anatomy alter the pharmacokinetics and subjective effects of ingested alcohol,[4] which contributes to the increased risk of AUD. However, results from previous studies are limited because: 1) blood alcohol concentrations (BAC) were measured in venous samples, which underestimates peak BAC delivered to the brain in patients who have had RYGB surgery, and 2) alcohol subjective effects have not been assessed using validated questionnaires. The purpose of the present study was to evaluate the effect of RYGB on the pharmacokinetics and subjective effects of ingested alcohol, by using arterialized blood samples and a validated questionnaire

Methods. Eight women who had RYGB surgery (RYGB+ group) within the last 1-5 yrs (mean 2.2±0.4 yrs) and 9 women scheduled to have RYGB surgery at Barnes-Jewish Hospital in St. Louis, MO (RYGB- group) provided written informed consent and participated in this study (Table), which was approved by the Institutional Review Board.

The study was conducted in the Clinical Research Unit (CRU) at Washington University School of Medicine. Fat-free mass (FFM) was determined by dual-energy X-ray absorptiometry. All subjects completed two sessions about 1 week apart, in which their response to alcohol or a nonalcoholic beverage was evaluated in a randomized cross-over fashion. For each session, subjects were admitted to the CRU after overnight fast. An intravenous catheter was inserted into a hand vein, which was heated to 50°C by using a thermostatically controlled box, to obtain arterialized venous blood. Subjects then consumed either 0.5 g/kg FFM of alcohol (equivalent to ~ two standard alcoholic beverages) or a nonalcoholic placebo beverage over 10 min. BAC were measured using headspace-gas chromatography and subjects' level of "drunkenness" were assessed with the Addiction Research Center Inventory [5] before and for several hours

after ingesting each beverage. Five subjects in the RYGB- group were retested at 9.7±1.6 months after RYGB surgery and 28±10% weight loss.

The statistical significance of values between groups and conditions was evaluated by using mixed ANOVAs.

Results. BAC increased faster, peak BAC was ~two-fold higher, total BAC area under the curve was ~1.5 times larger, and feelings of drunkenness were greater in the RYGB+ than in the RYGB- group (Figure; Table). The same effects were observed in the 5 subjects who were studied before and after RYGB surgery (Figure).

Discussion. The results from this study demonstrate that RYGB increases the rate of delivery of ingested alcohol into the systemic circulation, resulting in both earlier and higher BAC peaks and a greater feeling of drunkenness. The alteration in alcohol pharmacokinetics means that the peak in BAC achieved after consuming ~2 drinks in women who have had RYGB surgery resembles that observed after consuming ~4 drinks in women who have not had surgery[6].These findings have important public safety and clinical implications. The BAC in the RYGB+ group exceeded the legal driving limit for 30 min after alcohol ingestion, but never reached the legal driving limit in the RYGB- group. The peak BAC in the RYGB+ group also met the National Institute on Alcohol Abuse and Alcoholism criteria used to define an episode of binge drinking, which is a risk factor for developing AUD. These data underscore the need to make patients aware of the alterations in alcohol metabolism that occur after RYGB surgery to help reduce the risk of potential serious consequences of moderate alcohol consumption.

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Figure legend.

Blood alcohol concentrations (BAC) (panels A and C) and subjective feelings of drunkenness (panels B and D) after alcohol ingestion (0.50 g/kg FFM, which is equivalent to ~2 standard drinks) in women who had RYGB surgery (closed symbols) and in non-operated controls (open symbols). For each time point, scores on feelings of drunkenness on the alcohol day were subtracted from scores on the placebo day. Panels A and B show data on women who had RYGB surgery within the last 5 years (RYGB+; n=8) and in women who were scheduled to have RYGB surgery (RYGB-; n=9). Panels C and D show data from 5 subjects in the RYGB- group who repeated the studies at 9.7±1.6 months after RYGB surgery and 28±10% weight loss. *Value significantly different from RYGB- value or Before RYGB value, $P<0.05$ †Value significantly different from baseline value, $P<0.05$. Values are means ± SEM. Shown in red, the BAC limit for driving in the United States, which is also the BAC threshold for binge drinking defined by the National Institute on Alcohol Abuse and Alcoholism.

Table. Study subject characteristics.

	RYGB - (n=9)	RYGB + (n=8)	Longitudinal study (n=5)	
			Before RYGB	**After RYGB**
Age, mean (SD),yrs	41.1 (9.3)	42.5(8.0)	44.7 (4.6)	45.5 (4.7)
Weight, mean (SD),kg	120.2 (18.7)	80.8(14.1)[a]	109.3 (15.0)	79.1 (19.1)[b]
Body mass index, mean (SD),kg/m^2	44.1 (4.0)	30.0 (5.2)[a]	42.9 (4.7)	31.1 (6.9)[a]
FFM, mean (SD),kg	54.3 (6.0)	49.4 (5.7)	51.4 (5.8)	46.6 (5.8)[a]
Alcohol-related variables*				
Age 1^{st} drink, mean (SD),years	17.9 (3.0)	17.4 (2.3)	18.8 (4.0)	---
Age regular drinking, mean (SD),years	20.2 (2.8)	25.4 (10.6)	20.0 (3.7)	---
Drinking days per month (in last 6 months), mean (SD)	4.3 (4.7)	6.4 (5.7)	1.3 (0.4)	0.8 (0.8)
Drinks per drinking day (in last 6 months), mean (SD)	2.8 (1.5)	1.9 (1.7)	2.8 (1.6)	1.9 (2.4)
Number of standard drinks given on alcohol challenge test (SD)**	1.9 (0.2)	1.8 (0.2)	1.8 (0.2)	1.7 (0.2)
Peak BAC, mean (SD), $g \cdot l^{-1}$	0.60 (0.14)	1.10 (0.17)[a]	0.58 (0.09)	1.23 (0.2)[c]
Time to reach peak BAC, mean (SD), min†	35.6 (12.3)	15.0 (0.0)[a]	36.1 (15.8)	15.0 (0.0)[e]
Area under the BAC-time curve, mean (SD),$g \cdot l^{-1}$min	99.4 (6.8)	151.2 (7.2)[a]	99.3 (6.7)	173.5 (30.5)[d]

BAC=blood alcohol concentration

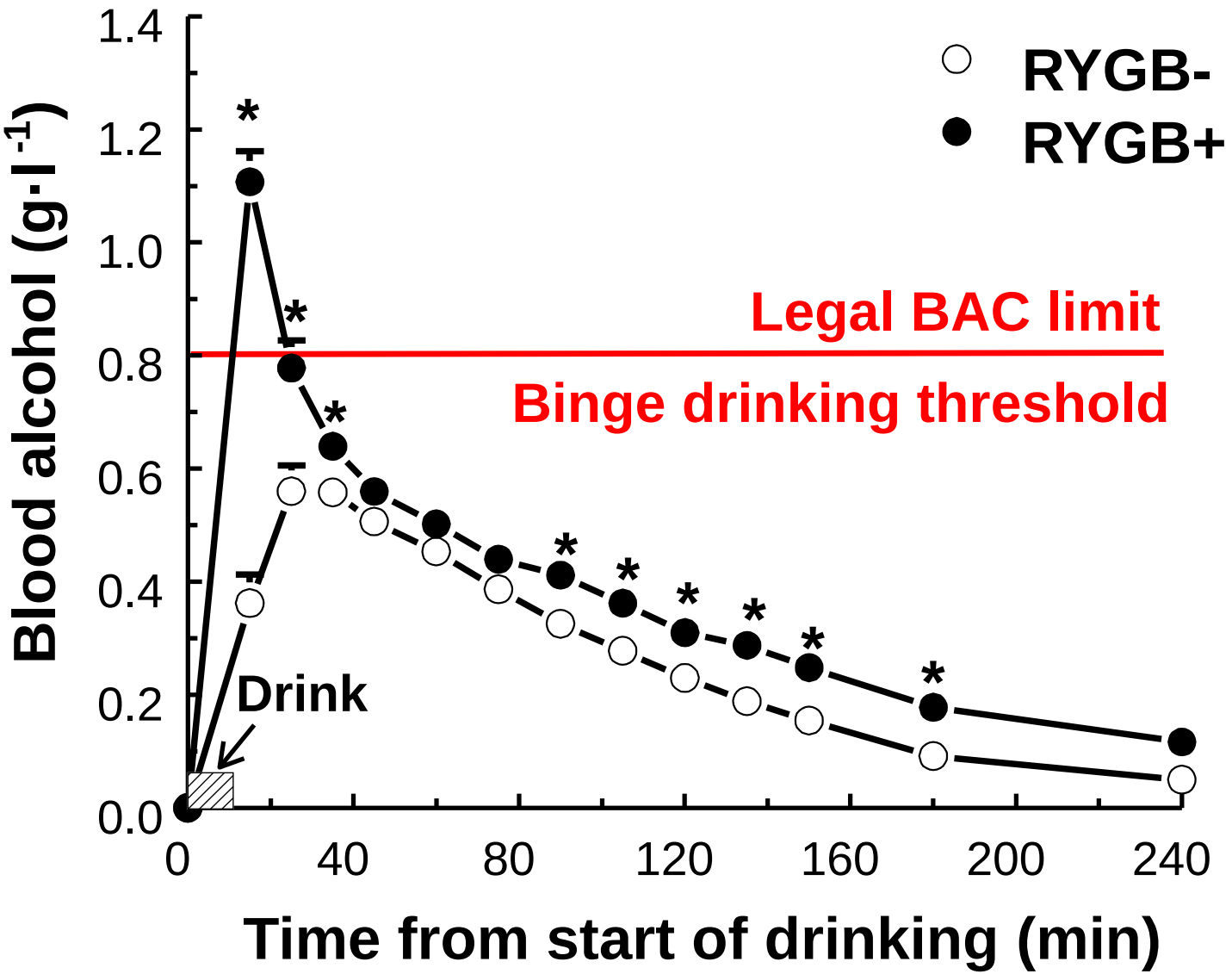
*The study is underpowered to detect clinically meaningful differences in history and pattern of alcohol use.

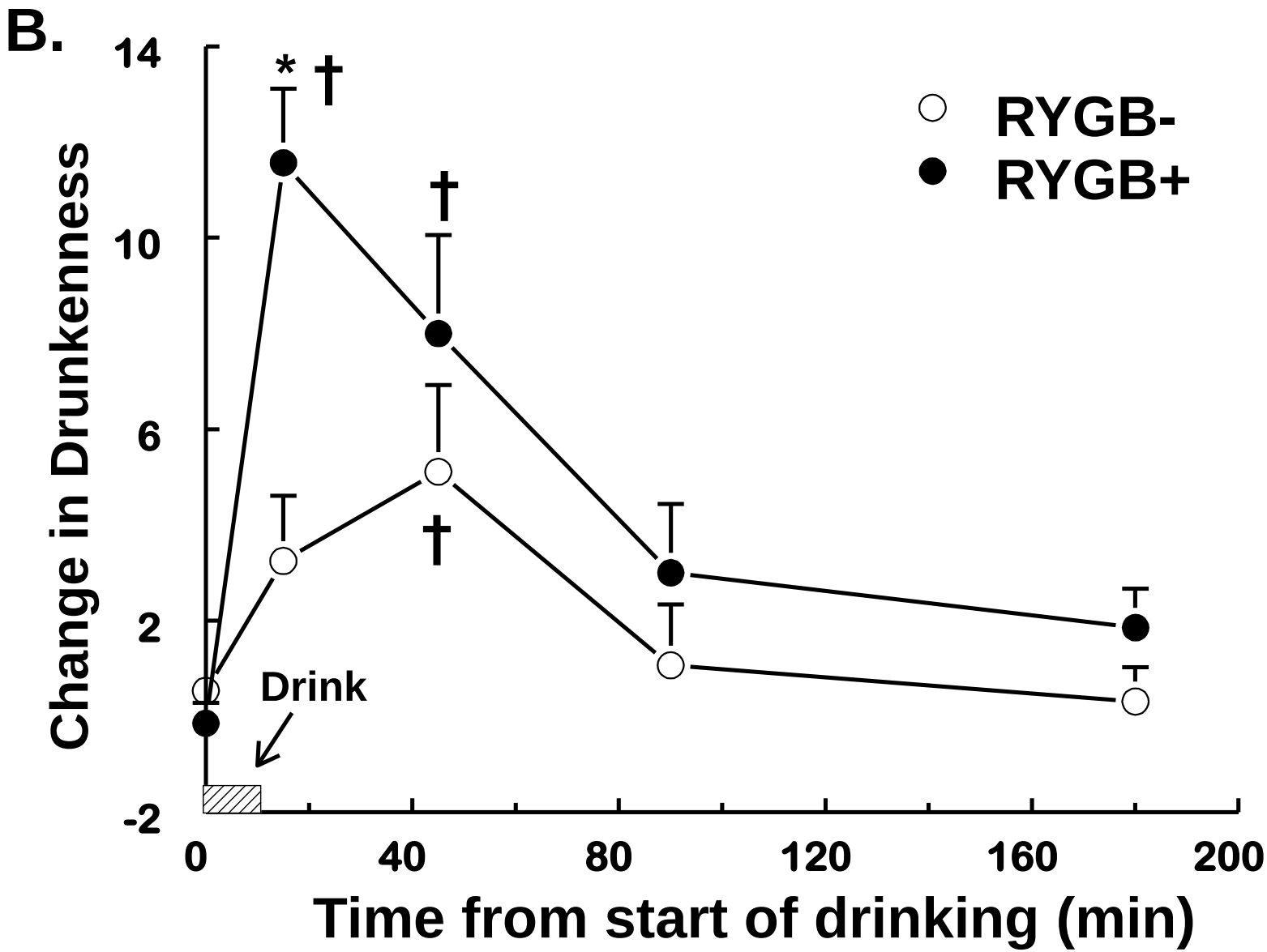
**One standard drink contains about 14 g of pure alcohol (about 17.7 ml of alcohol)

† Time to reach peak BAC is from the time of the first sip of alcoholic beverage, which was consumed over 10 minutes.

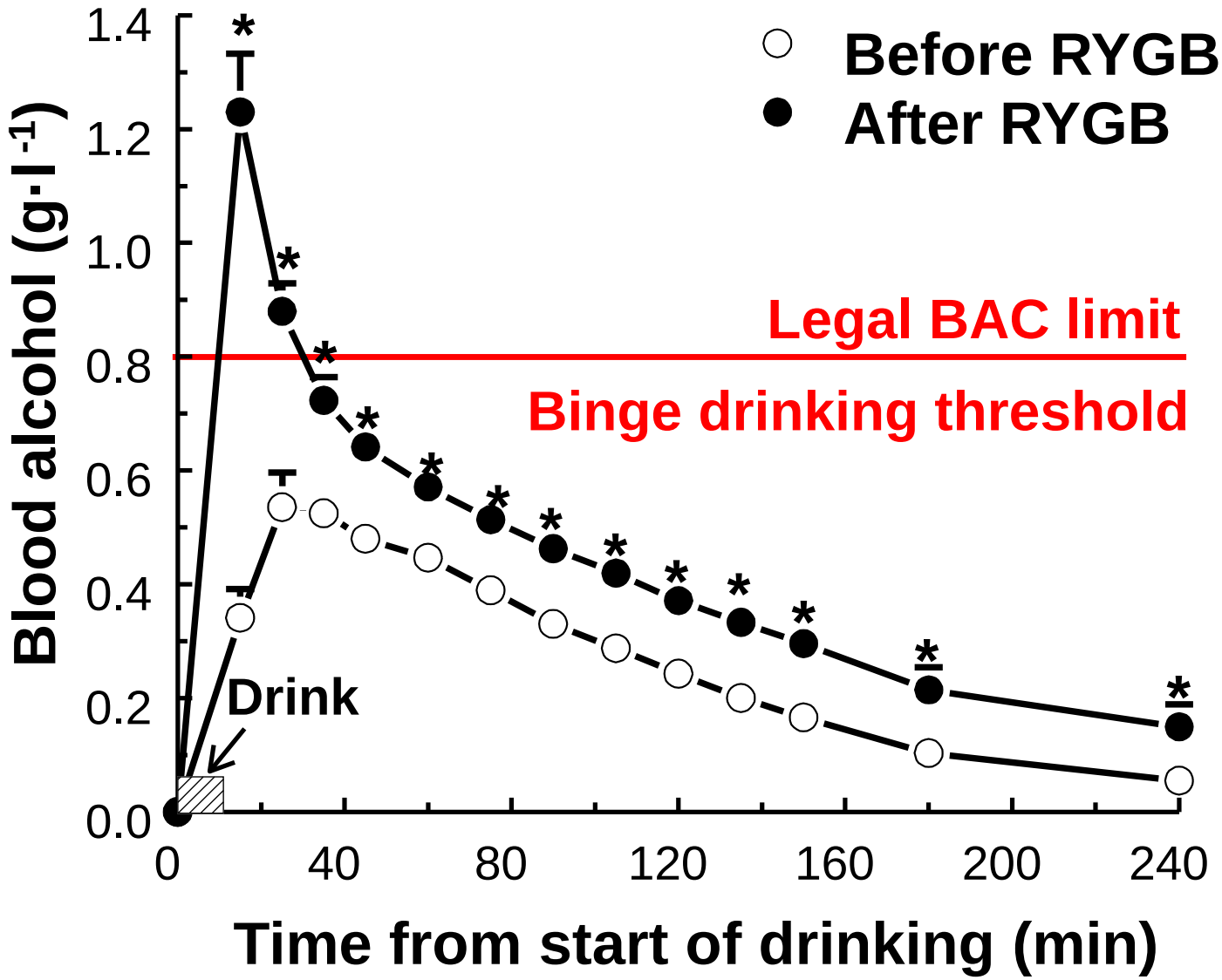
Value significantly different from corresponding RYGB- value or Before RYGB value, [a]P<.001, [b]P=.002, [c]P=.004, [d]P=.006, [e]P=.040

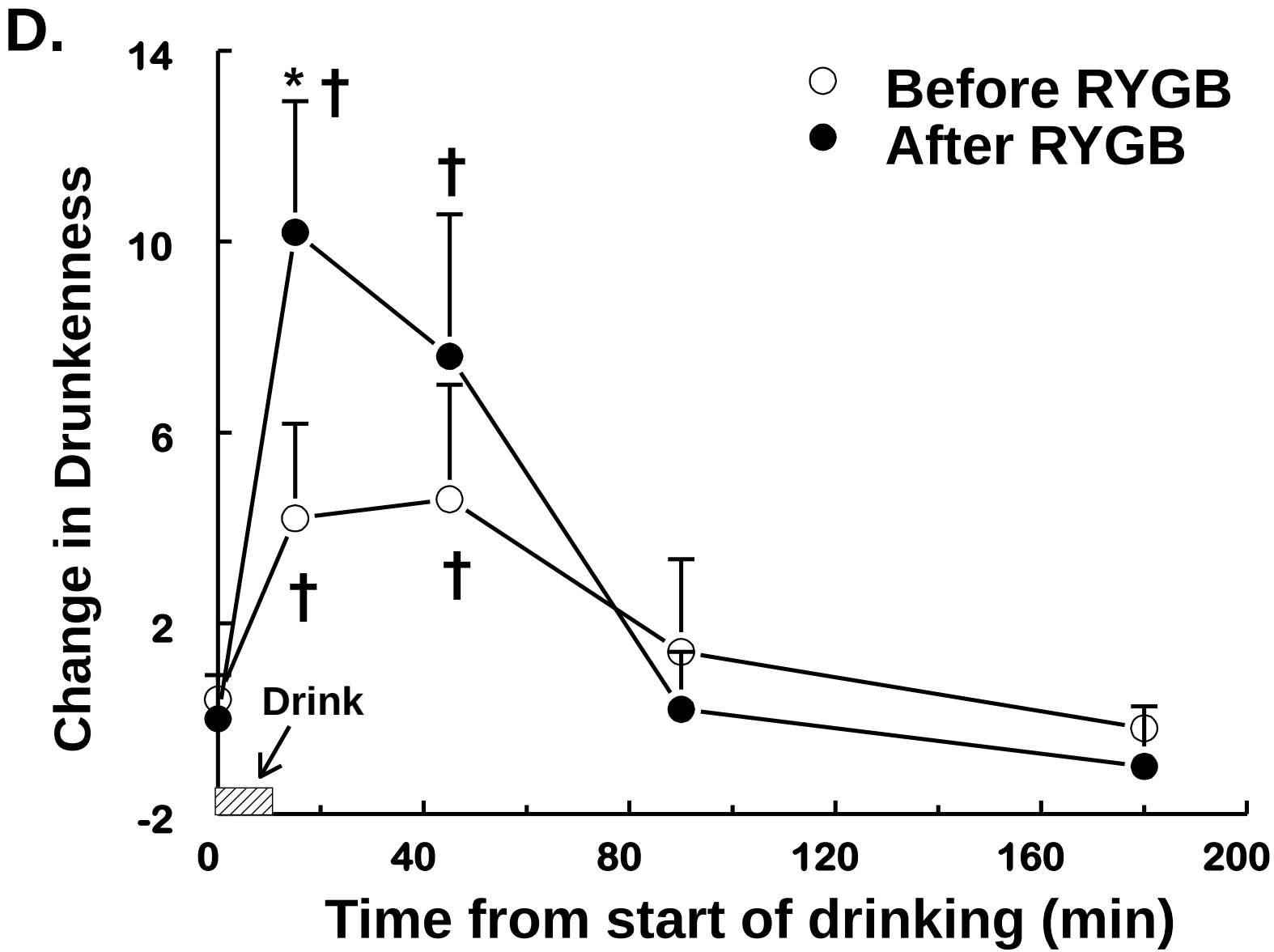
A.


RYGB-
RYGB+
Legal BAC limit
Binge drinking threshold
Drink
Blood alcohol (g·l-1)
Time from start of drinking (min)
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0
40
80
120
160
200
240
*


B.
14
10
6
2
-2
Change in Drunkenness
* †
†
†
RYGB-
RYGB+
Drink
0
40
80
120
160
200
Time from start of drinking (min)

C.


Before RYGB
After RYGB
Legal BAC limit
Binge drinking threshold
Drink
Blood alcohol (g·l-1)
Time from start of drinking (min)
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
0
40
80
120
160
200
240


D.
14
10
6
2
-2
Change in Drunkenness
Before RYGB
After RYGB
* †
†
†
†
Drink
0
40
80
120
160
200
Time from start of drinking (min)