No Effect of Sweetened Milk on Performance of a Battery of Cognitive Assessment Tests

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Introduction

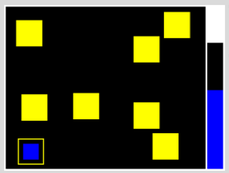
- Dietary sugar has been alleged to play a role in the development of cognitive dysfunction.
- Experimental procedures in which pure fructose is consumed, often at doses exceeding normal human consumption, may produce changes in cerebral activity and associated cognitive impairment.
- The practical implication of this is unclear, however, because of the rarity of pure fructose consumption in humans in isolation from other sugars and macronutrients.
- Therefore the purpose of this study was to test the effects of typical fructose consumption on cognitive function and compare the effects of pure fructose to fructose consumed from more common sources such as high fructose corn syrup (HFCS) or sucrose.

Methods

- All participants were apparently healthy and weight stable prior to enrollment (no change in weight >3% over the past three months; n=48, mean age 34.4 ± 11.1 years).
- Participants consumed sweetened or unsweetened low fat milk in amounts such that the added sugar contributed a target percentage of energy required for weight maintenance: fructose 9% (50th percentile of fructose consumption in the US), glucose 9%, high fructose corn syrup 18%, sucrose 18%; and an unsweetened milk control consumed such that milk contributed 18% of the weight-maintenance calories over a 10 week period.
- The energy intake required for weight maintenance was estimated for each participant using the Miflin St Joer equation and an appropriate activity factor determined by responses to a physical activity questionnaire.
- Before and after the intervention participants were assessed on a battery of tests that measure a wide variety of cognitive functions (CANTAB).
  - Spatial Working Memory (SWM), Intra-Extra Dimensional Set Shift (IED), Stop Signal Task (SST), Delayed Matching to Sample (DMS), Paired Associates Learning (PAL), and Rapid Visual Information Processing (RVP).
  - In addition, participants also performed the Iowa Gambling Test (IGT).
- Data presented are means ± SD.

Description of Tests and Results

Spatial Working Memory

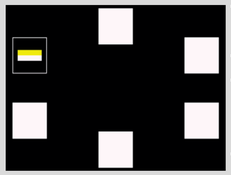


- A test of the subject's ability to retain spatial information and to manipulate remembered items in working memory.
- The subject must touch each box until a blue token is found. A new search will then commence with the token located in a box in which it has not yet been found. This will continue until the token has been successfully found in each of the boxes.

		HFCS 18%	Fructose 9%	Glucose 9%	Sucrose 18%	Unsweetened Milk	Pooled Population
Total Errors	Pre	28.9 ± 24.4	35.2 ± 25.2	16.3 ± 21.9	23.4 ± 25.1	24.7 ± 20.1	26.3 ± 23.2
	Post	30.9 ± 21.5	28.3 ± 27.7	24.9 ± 26.4	24.2 ± 25.2	16.1 ± 18.1	24.7 ± 23.3
Latency	Pre	885.7 ± 250.7	874.0 ± 290.1	830.5 ± 211.8	823.9 ± 135.5	812.1 ± 205.1	845.4 ± 217.4
	Post	899.3 ± 387.0	903.6 ± 299.2	757.5 ± 127.4	728.7 ± 143.7	670.2 ± 117.2	791.5 ± 253.7
Strategy	Pre	34.0 ± 5.8	35.5 ± 6.2	26.4 ± 8.0	32.4 ± 6.8	30.6 ± 7.7	32.1 ± 7.2
	Post	32.5 ± 5.8	32.9 ± 6.9	30.3 ± 9.5	30.1 ± 6.9	29.9 ± 6.2	31.2 ± 6.8

Measures
- Total Errors – The number of times a box is selected that is certain not to contain a token
- Latency – Mean time taken between token-search touches.
- Strategy – The most efficient strategy for completing the task is to follow a predetermined sequence for all searches. This is a measure of the number of times a subject begins a new search with a different box (scores range from 1-56). A lower score is better.

Paired Association Learning



- Boxes are displayed on the screen and are opened in a randomised order.
- One or more of them will contain a pattern.
- The patterns are then displayed in the middle of the screen, one at a time, and the participant must touch the box where the pattern was originally located.
- If the participant makes an error, the patterns are re-presented to remind the participant of their locations.
- The difficulty level increases through the test

		HFCS 18%	Fructose 9%	Glucose 9%	Sucrose 18%	Unsweetened Milk	Pooled Population
Total Errors	Pre	6.7 ± 5.1	12.0 ± 10.1	6.4 ± 6.1	6.9 ± 6.0	10.9 ± 15.8	8.8 ± 9.5
	Post	7.6 ± 5.8	7.8 ± 6.5	6.7 ± 7.3	6.4 ± 5.9	7.3 ± 9.2	7.2 ± 6.8
First Trial Memory	Pre	21.3 ± 3.2	19.8 ± 4.5	21.3 ± 4.8	20.7 ± 4.1	21.5 ± 3.0	20.9 ± 3.8
	Post	20.4 ± 3.4	20.6 ± 4.6	21.9 ± 3.7	21.8 ± 2.8	22.0 ± 3.8	21.3 ± 3.6
Stages Completed	Pre	8.0 ± 0.0	8.0 ± 0.0	8.0 ± 0.0	8.0 ± 0.0	7.9 ± 0.3	8.0 ± 0.1
	Post	8.0 ± 0.0	8.0 ± 0.0	8.0 ± 0.0	8.0 ± 0.0	8.0 ± 0.0	8.0 ± 0.0

Measures
- Total Errors – Total errors across all 8 stages
- Memory Scores – The number of patterns located after the first trial summed across all 8 stages (range from 0-26).
- Stages Completed – How many of the 8 stages were completed

Stop Signal Task

- An arrow will appear in the circle in the center of the screen
- Participants have a key pad with 2 buttons and are instructed to the button that corresponds with the direction of the arrow (Go).
- In the second half of the test a beep will sometimes follow the appearance of the arrow and participants are instructed to refrain from pressing the button on these trials (Stop).

		HFCS 18%	Fructose 9%	Glucose 9%	Sucrose 18%	Unsweetened Milk	Pooled Population
RT (ms)	Pre	179.9 ± 88.5	141.8 ± 39.9	146.9 ± 34.9	169.5 ± 48.6	186.1 ± 33.8	166.9 ± 54.7
	Post	193.2 ± 97.6	170.3 ± 33.7	186.1 ± 52.6*	150.4 ± 48.4†	167.1 ± 41.4†	172.5 ± 59.1
Successful Stops (%)	Pre	50.1 ± 13.1	51.2 ± 0.8	55.1 ± 0.8	58.7 ± 11.1	51.2 ± 10.4	53.3 ± 10.6
	Post	47.3 ± 11.7	55.1 ± 12.8	58.6 ± 0.8	55.3 ± 0.9	47.5 ± 0.8	52.2 ± 10.6
RT on Go (ms)	Pre	542.5 ± 191.7	476.2 ± 91.8	583.3 ± 213.6	532.8 ± 233.4	457.0 ± 149.0	513.8 ± 179.2
	Post	456.5 ± 123.8	460.9 ± 72.3	569.3 ± 195.9	516.7 ± 193.5	416.5 ± 106.8	477.6 ± 146.2*

* Different than baseline, p<0.05
† Change from baseline different than glucose 9%, p<0.05

Measures
- RT– Reaction Time (ms). This is an estimate of the length of the time between the go and stop stimuli that allows the participant to successfully inhibit pressing the button on 50% of the Stop trials.
- Successful stops – The percent success rate for participants correctly inhibiting the pressing of the button on a Stop trial.
- RT on Go – Mean Reaction time for pressing the button on Go trials.

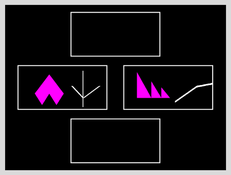
Rapid Visual Processing

- A sequence of numbers will be presented to the participant eg 3-5-7.
- Numbers from 2-9 will appear in the white box in the center of the screen and cycle at a rate of 100/minute.
- Participants are required to detect the target sequence, registering the identification on the keypad.

		HFCS 18%	Fructose 9%	Glucose 9%	Sucrose 18%	Unsweetened Milk	Pooled Population
Latency	Pre	462.4 ± 134.1	388.8 ± 74.6	369.7 ± 87.5	349.2 ± 58.2	31.9 ± 109.0	393.8 ± 100.9
	Post	415.2 ± 73.8	395.5 ± 88.4	400.0 ± 71.3	379.6 ± 73.9	385.0 ± 67.6	394.5 ± 73.3
A'	Pre	0.91 ± 0.06	0.94 ± 0.4	0.94 ± 0.04	0.96 ± 0.03	0.92 ± 0.07	0.93 ± 0.05
	Post	0.92 ± 0.06	0.95 ± 0.06	0.95 ± 0.05	0.96 ± 0.04	0.94 ± 0.05	0.94 ± 0.05

Measures
- Latency – Time taken to respond when correctly detecting the target sequence
- A' – The total measure of sensitivity to identifying the correct sequence, taking into account the probability of correctly identifying the sequence and the probability of a false positive identification.

Intra-Extra Dimensional Set Shift

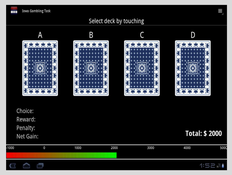


- The participant starts by seeing two simple color-filled shapes, and must learn which one is correct by touching it.
- Feedback teaches the participant which stimulus is correct, and after six correct responses, the stimuli and/or rules are changed.
- Participants progress through the test by satisfying a set criterion of learning at each stage (six consecutive correct responses).
- If at any stage the participant fails to reach this criterion after 50 trials, the test terminates

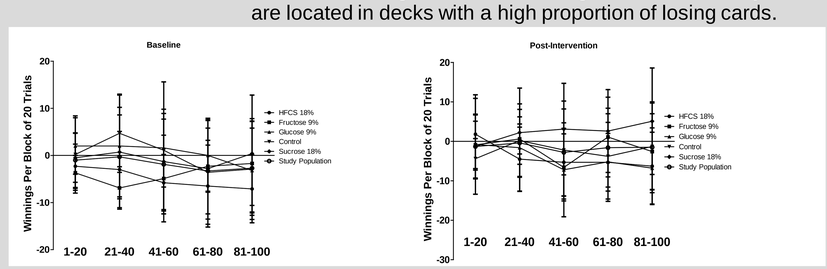
		HFCS 18%	Fructose 9%	Glucose 9%	Sucrose 18%	Unsweetened Milk	Pooled Population
Errors (Adjusted)	Pre	37.4 ± 25.5	23.6 ± 22.5	15.9 ± 12.1	23.1 ± 21.8	20.3 ± 19.2	24.5 ± 21.4
	Post	24.4 ± 21.4	19.5 ± 17.4	23.0 ± 24.2	18.6 ± 17.4	20.8 ± 20.0	21.1 ± 19.2
Stages Completed	Pre	8.0 ± 1.1	8.5 ± 0.8	8.9 ± 0.4	8.6 ± 0.8	8.6 ± 0.8	8.5 ± 0.9
	Post	8.5 ± 0.8	8.8 ± 0.6	8.6 ± 0.8	8.7 ± 0.7	8.6 ± 0.8	8.6 ± 0.7
Total Trials (Adjusted)	Pre	114.0 ± 41.2	96.4 ± 41.3	78.0 ± 19.8	92.6 ± 38.0	90.5 ± 35.1	95.2 ± 36.9
	Post	96.2 ± 38.4	84.8 ± 30.0	89.3 ± 40.0	83.9 ± 26.3	89.2 ± 34.1	88.7 ± 32.6

Measures
- Errors (Adjusted) – Total number of errors including penalty points for stages not reached due to early termination of the test.
- Stages Completed – Maximum of 9
- Total Trials (adjusted) - Total number of trials across all stages, including penalty points for stages not reached due to early termination of the test

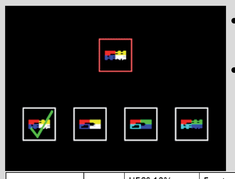
Iowa Gambling Test



- There are 4 decks of cards placed face down. Participants will select a card from one of the 4 decks on each of 100 trials.
- On each trial the selected card will either win or lose the participant "money"
- They are told that some decks are more profitable than others and the object is to earn as much money as possible over the 100 trials.
- Decks containing cards that win a high amount of money are located in decks with a high proportion of losing cards.



Delayed Matching Sample



- The participant is shown a complex visual pattern (the sample), then after a brief delay, four similar patterns
- The participant must then touch the pattern that exactly matches the sample

		HFCS 18%	Fructose 9%	Glucose 9%	Sucrose 18%	Unsweetened Milk	Pooled Population
Percent Correct	Pre	89.8 ± 6.1	90.0 ± 6.5	95.0 ± 2.9	94.0 ± 5.2	89.3 ± 7.9	91.4 ± 6.3
	Post	89.5 ± 4.0	89.2 ± 8.1	87.6 ± 4.2	92.0 ± 5.4	90.9 ± 4.1	90.1 ± 5.3*
Latency on Correct (ms)	Pre	3122.4 ± 583.0	2545.1 ± 671.1	3238.9 ± 498.3	2960.0 ± 683.3	3071.1 ± 1026.2	2982.7 ± 742.4
	Post	2886.3 ±605.2	2585.9 ± 547.3	2795.4 ± 387.9	2686.7 ± 442.5	2843.3 ± 774.4	2762.7 ± 569.6

* Different than baseline, p<0.01

Measures
- Percent Correct – Percent of trials in which the correct response was selected on the first attempt
- Latency on Correct – The time taken to make a selection on trials in which the correct options was selected.

Discussion & Conclusion

- These data suggest that when fructose is consumed in the amounts and manner in which is typical in the human diet, previously reported changes in cognitive function are not observed.
- As such, these previous observations may to due to experimental conditions that do not reflect real life settings.

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