

Chronic Methamphetamine Abuse and Early Onset of Type 2 Diabetes

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Abstract

The human brain controls the overall functioning of the body with brain signaling. Some current research on Type 2 diabetes suggests the disease may be caused from the brain not signaling properly. Chronic methamphetamine use is associated with many adverse health problems that are the result of repeated exposure to the substance. Much of the research on chronic methamphetamine use repeatedly finds it causes damage to the Dopamine (DA), Serotonin (SN), and norepinephrine (NE), neurotransmitters. The chronic methamphetamine user is subjected to neurotransmitter changes that are similar to those in type 2 diabetes. There is a great need to early diagnose Type 2 diabetes and to test this target group that may be at a higher risk for developing the disease. The hypothesis for this research is that the chronic methamphetamine user will be more likely to have higher blood glucose levels associated with Type 2 diabetes.

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A large amount of research has found that the drug methamphetamine acts primarily on the pleasure center of the brain's mesolimbic dopaminergic pathway. It increases the brain's levels of dopamine (DA) up to eight times higher than normal. This large amount of DA causes a euphoric sensation and the reason it is called the pleasure pathway. This drug also has a strong influence on one's overall motivation and this may influence a person's desire to quit. This reward pathway influences our cravings, motivation, eating, energy and overall brain functioning (Chesworth, Brown, Kim, Ledent, & Lawrence, 2015). There is little research that has studied methamphetamine's effect on the brain's energy homeostasis and the topic of this research is to examine it after chronic methamphetamine use.

Typically we think of obesity and a poor diet as the lifestyle factors that contribute to Type 2 diabetes but chronic methamphetamine abuse may also contribute to the disease. There are special neurons that regulate energy by sensing glucose and signaling insulin (Stephans & Yamamoto, 1995). Overtime the insulin receptors become desensitized to methamphetamine and less insulin is secreted (Bayat & Haghparast, 2015). Research has found that chronic methamphetamine use damages the dopaminergic neurotransmitter, leaving little or no DA production (Chang, Alicata, Ernst, & Volkow, 2007). This can cause a person's to have symptoms similar to Parkinson's disease. These include excessive drowsiness, binge eating, difficulty regulating mood and sleep problems. One study conducted by Chan-Palay (1990) concluded that many of these symptoms occur from a communication breakdown at the DA neurotransmitter. In this state the body becomes misinformed and begins to change its functioning to adjust to the different neuronal and chemical environment (Scarlett & Schwartz, 2015).

The brain needs about 20% of all the body's energy and gets this from absorbing glucose from the blood (Mao, Brinton, Schneider, & Zhao, 2013). A large part of the brain's energy is closely related to its metabolism by which it processes glutamate. The brain uses insulin, DA and other hormones to process glucose (Chaput & Tremblay, 2008). First the blood delivers glycogen to the blood brain barrier and for a few minutes stores it in astrocyte glia cells until it is synthesized into the glutamate it can use as energy (Snider, Hendrick, & Beardsley, 2013). Most research agrees that the optimal condition for the brain is normal sugar and low insulin. Mayer theorized that energy homeostasis was being regulated by special glucose sensing receptors in the ventromedial hypothalamus (VMH). When these receptors sensed the blood glucose getting too low it would signal the release of ghrelin, a hormone that makes someone feel hungry (Lawrence, 2002). The research by Stephens & Yamato (1995) suggested abnormal glutamate homeostasis may also be a contributing factor to developing type 2 diabetes. DA receptors in dopaminergic cells detect DA molecules outside of cell and activate a response. The size of the response depends on the number of receptors. With repeated stimulation from methamphetamine the DA receptors become less sensitive. This leads to a decreased functioning (Huber, Ling, Shoptaw, Gulati, Brethen, Rawson, 1997). This occurs within the Nucleus accumbens and diabetes is related to less DA in that same area (Yang, 2011). Many dopaminergic pathways are impacted with methamphetamine use. In one research study done by J. Druker, he found that methamphetamine use interfered with DA's synthesis into nor-epinephrine (NE) (2015). One function of NE is that it triggers the glucose release from stored energy. In another study the researchers concluded that the NE also relays regenerating information from the brain to the islet cells in the pancreas (Drucker, 2015).

The brain insulin regulates glucose sensing and the counter-regulatory responds to

hypoglycemia (Dietrich & Horvath, 2012). During Type 2 diabetes the major barrier in blood glucose homeostasis is the impaired ability to sense and respond to insulin. The research by Mao, Brinton, Schneider, & Zhao (2013) found damage to the insulin receptors in the brain caused impaired sensing. These brain regions have proven to influence regulation of food intake and related dopamine reward pathways. Another study found the neurons became more sensitive to meth and found cells used fatty acid oxidation as an alternative source of energy during the glucose limitation (Yang, 2011). Stimulants activate the brain's sympathetic response. While in this flight or fight mode nor-epinephrine (NE) is released from receptors. Additionally, glycogen is converted into glucose and insulin is released that helps glucose enter the cells (Stephans & Yamamoto, 1995). Too much or too little insulin can influence our behavior and can have an effect on how the brain functions. Methamphetamine is known to stimulate production of insulin, which leaves the blood hypoglycemic (McMahon, Andersen, Feldman, & Schanberg, 1971).

A person's hunger is related to intake of glucose, energy and may cross over to the reward pathways involved with substance abuse. Furthermore, laboratory studies on addiction have found that an animal's anticipatory behavior could be modified and their preferred place preference reversed by the administration of insulin (Bayat & Haghparast, 2015). The results are similar with people and food addiction (Florant et al., 1991). Many people believe that sugar is a stimulant and binge eating sugary foods can affect the reward pathway in a similar way that methamphetamine use does. In fact sugar enters almost as fast and causes body tissues to uptake glucose and the pancreas to release insulin. These types of spikes can make cells no longer respond to the insulin and you can develop type 2 diabetes (Ehrenberg, 2012). Both substances act on the same neurotransmitters.

Methamphetamine addiction is a terrible disease that stems from our brain's reward pathway being hijacked by a powerful force that is influencing the desire to stop (Chesworth, Brown, Kim, Ledent, & Lawrence, 2015). A person can experience “cross-sensitization” from sugar to drugs of abuse and this causes the user to relapse. Many addicts struggle with the problem for many years. The chronic methamphetamine user has most likely damaged some brain cells and over time it has changed how their body works (Chang, Alicata, Ernst, & Volkow, 2007). Some of these people will not fully recover from the damage the drug has caused (Volkow, Chang, Wang, Fowler, Franceschi, Sedler, Gatley, Miller, Hitzemann, Ding, & Logan, 2001).

In the current research study it is hypothesized that the chronic methamphetamine user will have higher blood glucose levels similar to people with type 2 diabetes.

Method

Participants

After obtaining institutional ethical committee clearance and facility clearance only participants who are over the age of 18 will be selected. The facility is the Ventura County Department of Alcohol and Drug Treatment Program located at 24 East Main Street in Ventura, California. This location is where people are referred to from within Ventura County and it conducts many drug treatment programs in a group style. The willing participants will be screened and selected. A total of 60 patients (both male and female, age range 18 to 69 years) are selected from people in the outpatient treatment.

Materials

The glucose monitoring requires the following materials: A box of 100, 28 gauge B-D

Ultra-Fine lancet from Becton-Dickinson. An Accu-Check Compact plus Blood Glucose Monitoring System. A Bio hazard Sharps disposal container. A box of 100 count Latex gloves. A 100 count box of alcohol free Diabetic finger testing wipes. The target group will be screened and selected using a Likert style questionnaire. The instructions are written on top of the form as follows; Circle the most appropriate answer that describes them on each of the following: 1. Male / Female 2. Circle your age group, 18-30 and 31-up. 3. Circle how long have you used? 0-10 years, 11-up. 4. Do any of your family members have Type 2 diabetes? (Yes/No)

The informed consent will be obtained from all the participants in the study. Each participant is to be fully informed of the research purpose and any risks using the following information typed on the consent form. This diabetes screening is to study chronic methamphetamine use and if it contributes to the onset of type 2 diabetes. The blood glucose test is a meter and the results will be recorded anonymously. There is minimal risk of infection at the prick site. The results are simply recorded anonymously. If a participant is concerned about the results they must talk to their personal physician about it. Every participant will receive their results and will be immediately destroyed. A signature will be collected by each participant.

Procedure

The glucose blood test is to be carried out using capillary finger-pricks and results are immediately given while participant is present. Testing will only be administered by individuals that have undergone proper training and infection prevention during blood glucose monitoring according to the Center of Disease control's safety recommended procedures (2015). This includes wearing latex gloves and disposing them after each use. An auto-disabling single-use lancet devices is used for monitoring the blood glucose. Each lancet device will be disposed of properly in the sharps disposal container (Klonoff & Perz, 2010). The Glucose self-monitoring

device will be used according to the manufacturer's recommendations. Additionally, non-alcohol prep wipes are used to wipe off finger before test. A bandage is placed on testing site after test and results are given to each participant. For the research the blood glucose results are recorded on each questionnaire.

The total number of results are divided in two groups. One group is identified as being at relatively higher risk in relation to length of chronic methamphetamine use and age. The 18 to 30 year olds and the over 30 age are then sub-divided into groups according to length of time used. IBM SPSS Statistical analysis is to be completed using a correlational analysis method. The data will contain all of the demographic information collected on each questionnaire along with the blood glucose results for each person. Primarily the purpose of this study is to compare the subject's blood glucose levels with their age and length of using methamphetamines.

Conclusion

In this research study we hypothesize to find a pattern of higher glucose levels in the chronic user. This may be a useful for early detection of type 2 diabetes in this specialized groups. One weakness of this study is that many people develop Type 2 diabetes as a result of a combination of contributory factors. It is hard to determine if chronic methamphetamine use will likely be the only cause. Additionally the finger prick test is not performed on an empty stomach and is not the optimal condition. Future research in this area may want to ask more specific questions relating to how they took the drug because this may cause different long term physiological changes.

Works Cited

- Bayat, A.-H., & Haghparast, A. (2015). Effect of insulin deficiency on the rewarding properties of methamphetamine in streptozotocin-induced diabetic rats. *Pharmacology Biochemistry and Behavior*, 128, 8–13. <http://doi.org/10.1016/j.pbb.2014.11.008>
- Chan-Palay, V. (1990). Neuronal communication breakdown in neurotransmitter systems in Alzheimer's and Parkinson's dementias. *Journal of Neurocytology*, 19(5), 802–806. <http://doi.org/10.1007/BF01188047>
- Chang, L., Alicata, D., Ernst, T., and Volkow, N., Structural and metabolic brain changes in the striatum associated with methamphetamine abuse. *Addiction* 102:16–32, 2007.
- Chaput, J., & Tremblay, A. (2008). The glucostatic theory of appetite control and the risk of obesity and diabetes. *International Journal of Obesity* (2005). 1(33). Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/19002144>
- Chesworth, R., Brown, R., Kim, J., Ledent, C., & Lawrence, A. (2015). Adenosine 2A receptors modulate reward behaviors for methamphetamine. *Addiction Biology*. <http://doi.org/10.1111/adb.12225>
- Dietrich, M., & Horvath, T. (2012). Fat incites astrocytes to neurogenesis. *Nature Neuroscience*, 15(5), 651–653. <http://doi.org/10.1038/nn.3091>
- Drucker, D. J. (2015). Deciphering Metabolic Messages From the Gut Drives Therapeutic Innovation: The 2014 Banting Lecture. *Diabetes*, 64(2), 317–326. <http://doi.org/10.2337/db14-1514>
- Ehrenberg, R., (2012). Body & brain taste of fructose revs metabolism Pancreas cells pump more insulin in response to sugar. *Science News*, 181(7), 16-16. <http://doi.org/10.1002/scin.5591810718>

- Florant, G., Singer, L., Scheurink, A., Park, C., Richardson, R., & Woods, S. (1991). Intra ventricular insulin reduces food intake and body weight of marmots during the summer feeding period. *Physiology & Behavior*, *49*(2), 335–338.
[http://doi.org/10.1016/0031-9384\(91\)90053-q](http://doi.org/10.1016/0031-9384(91)90053-q)
- Huber, A., Ling, W., Shoptaw, S., Gulati, V., Brethen, P., and Rawson, R. Integrating treatments for methamphetamine abuse: A psychosocial perspective. *J Addiction* *16*(4):41–50, 1997.
- Infection Prevention during Blood Glucose Monitoring and Insulin Administration. Retrieved 24 April 2015, from <http://www.cdc.gov/injectionsafety/blood-glucose-monitoring.html>
- Klonoff, D., and Perz, J. Assisted Monitoring of Blood Glucose: Special Safety Needs for a New Paradigm in Testing Glucose *J Diabetes Sci Technol* *2010.4*(5):1027-1031
- Lawrence, D. (2002). Researchers uncover hormone that turns off hunger switch. *The Lancet*, *360*(9331). [http://doi.org/10.1016/s0140-6736\(02\)09700-3](http://doi.org/10.1016/s0140-6736(02)09700-3)
- Mao, Z., Brinton, R., Schneider, L., & Zhao, L. (2013). Estrogen receptor- β regulation of insulin signaling and energy metabolism in APOE- ϵ 2, ϵ 3, ϵ 4 brains. *Alzheimer's & Dementia*, *9*(4). <http://doi.org/10.1016/j.jalz.2013.05.6>
- Mayer, J. (1953). Glucostatic Mechanism of Regulation of Food Intake. *New England Journal of Medicine*, *249*(1), 13–16. <http://doi.org/10.1056/nejm1953>
- Mcmahon, E., Andersen, D., Feldman, J., & Schanberg, S. (1971). Methamphetamine-Induced Insulin Release. *Science* *174*(4004), 66–68. <http://doi.org/10.1126/science.174.4004.66>
- Reinehr, T., & Roth, C. L. (2015). The gut sensor as regulator of body weight. *Endocrine*, *49*(1), 35–50. <http://doi.org/10.1007/s12020-014-0518-1>
- Scarlett, J., & Schwartz, M. (2015). Gut-brain mechanisms controlling glucose homeostasis. *Prime Reports*. <http://doi.org/10.12703/p7-12>

- Snider, S., Hendrick, E., & Beardsley, P. Glia cell modulators attenuate methamphetamine self-administration in the rat. *Journal of Pharmacology* 701(1-3):124-130, 2013.
- Stephans, S., & Yamamoto, B. (1995). Effect of repeated methamphetamine administrations on DA and glutamate efflux in rat prefrontal cortex. *Brain Research* 700(1-2), 99-106...[http://doi.org/10.1016/0006-8993](http://doi.org/10.1016/0006-8993(95)00938-m) (95)00938-m
- Volkow, N., Chang, L., Wang, G., Fowler, J., Franceschi, D., Sedler, M., Gatley, S., Miller, E., Hitzemann, R., Ding, Y., & Logan, J. Loss of DA transporters in methamphetamine abusers recovers with protracted abstinence. *J Neuroscience* 21(23):9414-9418, 2001.
- Yang, Y.-Q. (2011). Alteration of the proteome profile of the pancreas in diabetic rats induced by streptozotocin. *International Journal of Molecular Medicine*.
<http://doi.org/10.3892/ijmm.2011.696>