Methamphetamine (MA) is an increasingly popular illegal stimulant in the United States. Smoking MA has increased in popularity since it causes a rapid and sustained high. When MA is smoked, a pyrrole product, proto-phenylpropene (TPP), is produced. The mechanisms responsible for the physiological effects of MA on the lung (increased airway resistance, asthma-like symptoms of reduced airflow) and the relative contributions of MA and TPP to the lung effects are unknown. Therefore in this study, the effects of MA were tested in two different models, in vivo and in vitro.

Respiratory and cardiac natriuretic peptide (ANP) have been shown to be the cytokine IL-1β has been shown to be secreted. IL-1β is the dual pathway-activation of the NLRP3 inflammasome that is inhibited by MA. If these proteins have elevated levels in people with moderate to severe asthma (ANP-Mohapatra et al., 2004) (Resistin-LaRochelle et al., 2007). If these proteins are found in MA and TPP treated lung samples, a protease control. A MTIS array was used to determine the presence of the chemicals on the cells, and IL-1β levels were measured using an ELISA kit. MA and TPP were not found to be significantly toxic to cells. However, both MA and TPP were found to decrease IL-1β production, consistent with the reported effect of MA on the immune system.

Results

Airway epithelium acts as a physical barrier against inhaled particles, as well as producing pro-inflammatory cytokines as part of an immune response. One of the symptoms of asthma is bronchial constriction, which can be caused by smooth muscle contraction or airway inflammation.

Methods

Human Cell Line

The cells used in this experiment were human THP-1 monocyte cells. The cells were cultured in 1640 RPMI with 10% fetal bovine serum. Cells were differentiated into macrophages 24 hours before use by adding phorbol ester (PMA).

Histology and Immunohistochemistry

Paraffin embedded lungs of DO11.10 mice with a BALC background were sectioned on a microtome into 7 μm sections. Lung sections were stained using an ABC Vectastain kit and an ImmunoBeads DAB Peroxidase Substrate, both from Vector Laboratories and used according to manufacturer's protocol.

Future Directions

• Determine the specific component of the inflammasome that is inhibited by MA.

References

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**Abstract**

Methamphetamine (MA) is the most widely used illegal stimulant in the United States. Smoking MA has increased in popularity since it causes a rapid and sustained high. When MA is smoked, a pyrrole product, proto-phenylpropene (TPP), is produced. The mechanisms responsible for the physiological effects of MA on the lung (increased airway resistance, asthma-like symptoms of reduced airflow) and the relative contributions of MA and TPP to the lung effects are unknown. Therefore in this study, the effects of MA were tested in two different models, in vivo and in vitro.

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**Introduction**

Methamphetamine (MA) is the most widely used illegal stimulant in the United States according to a 2006 National Drug Intelligence Center report. The number of users has been steadily increasing over the last 14 years nationwide. The National Drug Threat Assessment Report stated that smoking is the leading mode of administration, and it produces an almost instantaneous and long-lasting high. When MA is heated in the process of smoking, some of the solid is chemically broken down, forming a pyrrole product proto-phenylpropene (TPP). Once inhaled, TPP is metabolically activated into an epithile that causes cell degradation and death (Singh et al., 2005).

The effects of MA on the central nervous system have been well-documented and continue to be investigated; however, the effects on the respiratory system have not been thoroughly studied.

It has been noted that people who have been indirectly exposed to MA present asthma-like symptoms (Sarac et al., 2009). In a recent study, it was found that acute exposure to a smoke containing MA caused lung injury in mice (Hollan et al., 2008). Unpublished microscopic analysis from the same study showed that in lung tissues from mice exposed to MA, the mRNA of two proteins, atrial natriuretic peptide (ANP) and resistin were upregulated. The mechanisms responsible for the physiological effects of MA on the lung (increased airway resistance, asthma-like symptoms of reduced airflow) and the relative contributions of MA and TPP to the lung effects are unknown. Therefore in this study, the effects of MA were tested in two different models, in vivo and in vitro.

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**In Vivo Model**

Airway epithelium acts as a physical barrier against inhaled particles, as well as producing pro-inflammatory cytokines as part of an immune response. One of the symptoms of asthma is bronchial constriction, which can be caused by smooth muscle contraction or airway inflammation.

**In Vitro Model**

Antiviral factors are induced in respiratory epithelial cells. Once phagocytosed, macrophages can secrete pro-inflammatory cytokines in response to infection, which can lead to increased inflammation.

**Cytokine Measurements**

In vitro models of MA and TPP to the lung effects are unknown. Therefore in this study, the effects of MA were tested in two different models, in vivo and in vitro.

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**Acknowledgements**

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