Tetramethylenedisulfotetramine Neurotoxicity: In Vivo Validation of In Vitro Screen to Identify Potential Countermeasures

Marcela Laukova  
New York Medical College

Sundas Pervez  
New York Medical College

Fatim Sannoh  
New York Medical College

Jana Veliskova  
New York Medical College

Libor Velisek  
New York Medical College

See next page for additional authors

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Authors
Marcela Laukova, Sundas Pervez, Fatim Sannoh, Jana Veliskova, Libor Velisek, and Michael Shakarjian

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Numerous drugs are known to counteract TMDT-induced seizures and lethality. In fact, we have identified compounds that can reverse the toxic effects of TMDT and other GABAergic neurotoxins. Our approach may be particularly significant in cases of sudden accidental or intentional exposure to various neurotoxic agents inducing lethal seizures with concurrent rise of \([\text{Ca}^{2+}]_i\) and the need to establish accurate dosing.


**CONCLUSIONS**

- Drugs of the same pharmacological class, such as NMDAR antagonists, failed to display any significant improvements upon administration of TMDT and other GABAergic neurotoxins.
- No neuronal death has been observed 24 hr following TMDT treatment in vivo or in vitro.
- Our in vitro monitoring of \([\text{Ca}^{2+}]_i\) fluxes represents a valid and useful medium-throughput screening tool to evaluate potential effective treatments for TMDT and other GABAergic neurotoxins in vivo.
- Exploitation of our in vitro approach may be particularly significant in cases of sudden accidental or intentional exposure to various neurotoxic agents inducing lethal seizures with concurrent rise of \([\text{Ca}^{2+}]_i\) and the need to promptly identify effective treatments.

**Acknowledgements:** NIH Career-Development Award (5K02NS059050-03) for financial support and Drs. Jared Alder and Smita Varia of Robert Wood Johnson Medical School, Rutgers University, for assistance with tissue dissections.