

Enhanced prediction and prevention of drug-induced torsades de pointes

Citation for published version (APA):

Johnson, D. M. (2013). *Enhanced prediction and prevention of drug-induced torsades de pointes*. BOXPress. <https://doi.org/10.26481/dis.20130308dj>

Document status and date:

Published: 01/01/2013

DOI:

[10.26481/dis.20130308dj](https://doi.org/10.26481/dis.20130308dj)

Document Version:

Publisher's PDF, also known as Version of record

Please check the document version of this publication:

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Enhanced Prediction and Prevention of Drug-Induced Torsades de Pointes

Daniel Johnson, 8 March 2013

1. Calcium-induced and spontaneous calcium release from the sarcoplasmic reticulum are key determinants of beat-to-beat variability of repolarization in the cardiac myocyte. (This thesis)
2. The potassium current I_{Ks} plays a vital role in preventing excessive beat-to-beat variability of repolarization during β -adrenergic stimulation. (This thesis)
3. Apart from causing triggered activity, delayed afterdepolarizations and the underlying calcium mechanism can contribute to arrhythmia formation by exaggerating regional and temporal dispersion of repolarization. (This thesis)
4. Preventing late-diastolic spontaneous calcium release by different drug actions reduces beat-to-beat variability of repolarization and proarrhythmia, especially during β -adrenergic stimulation. (This thesis)
5. Combined ion-channel blockade can provide safer antiarrhythmic treatment than conventional drugs, but the balance of block is of utmost importance. (This thesis)
6. Adrenergic stimulation can lead to cardiac aftercontractions that are involved in the triggering of torsades de pointes in patients with long-QT1 syndrome.
7. Cardiac safety pharmacologists and drug regulators should look beyond hERG block and QT prolongation when assessing proarrhythmic risk.
8. Prediction is very difficult, especially about the future. (*Niels Bohr*)
9. He who speaks a bit of a foreign language has more delight in it than he who speaks it well; pleasure goes along with superficial knowledge. (*Friedrich Nietzsche*)
10. By seeing the seed of failure in every success, we remain humble. By seeing the seed of success in every failure we remain hopeful. (*Paul J. Meyer*)
11. Sleep is a symptom of caffeine deprivation. (*Author unknown*)