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MEETING ABSTRACT

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Anti-addiction drug ibogaine and the heart: a delicate relation

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Background: Ibogaine is an indole alkaloid derived from the African shrub *Tabernanthe iboga*. Although never licensed as therapeutic drug, ibogaine is used as anti-addiction medication in dozens of alternative-medicine clinics worldwide. Recently, alarming reports of QT-interval prolongation in the electrocardiogram, life-threatening cardiac arrhythmias, and sudden death cases associated with the ingestion of ibogaine have been accumulating.
Methods: In order to estimate the cardiac risk connected with ibogaine intake, we assessed the effects of the drug and its long-lived active metabolite noribogaine on cardiac ionic currents and action potentials (APs). Therefore, by using the whole-cell patch-clamp technique, currents from tsA cells expressing human cardiac ion channels, and APs from human induced pluripotent stem cell-derived ventricular-like cardiomyocytes were recorded.
Results: We report that therapeutic concentrations of ibogaine significantly inhibit human ether-a-go-go-related gene (hERG, $hK_V11.1$) potassium channels, and retard action potential repolarization in human cardiomyocytes. The latter finding represents the first direct experimental proof that ibogaine application implies a cardiac arrhythmia risk for humans. In addition, we found that noribogiane also inhibits hERG channels and prolongs the human cardiac AP in similar concentrations as its parent drug ibogaine. These results explain the clinically observed delayed incidence of cardiac adverse events sometimes even several days after ibogaine intake.
Discussion: The use of ibogaine as anti-addiction drug is associated with a cardiac arrhythmia risk due to hERG channel block. Hereby, noribogaine may represent the main player responsible for long-term cardiac toxicity after ibogaine ingestion. If considered an indispensable drug for anti-addiction therapy, we urge the responsible medical regulatory authorities to specify adequate standards and exclusion criteria to pave the way for a safer ibogaine anti-addiction therapy in the future.
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