

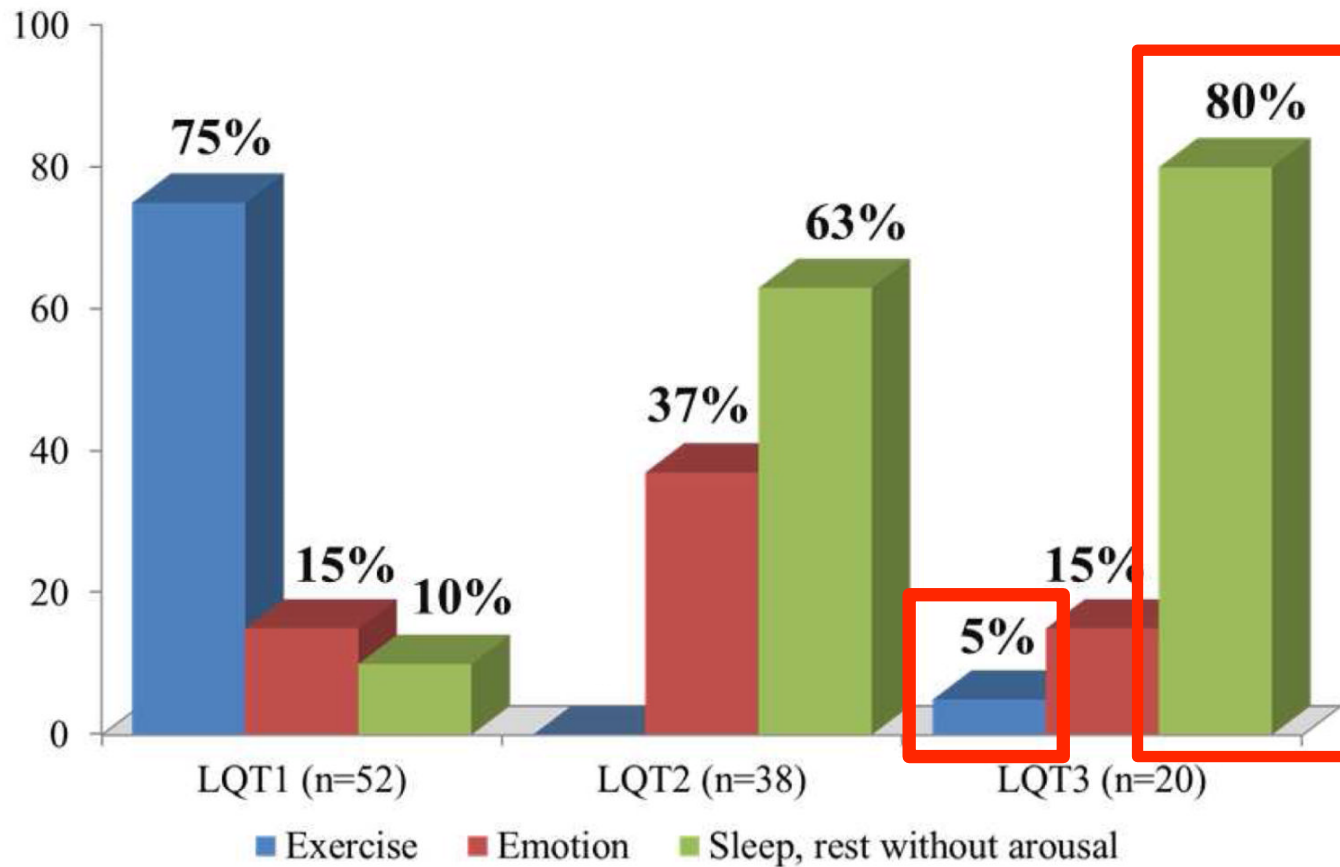
# Ventricular tachyarrhythmia provoked by exercise in pediatric patients with type 3 congenital long QT syndrome

- 1) Department of Pediatric Cardiology, National Cerebral and Cardiovascular Center
- 2) Department of Cardiovascular Medicine, National Cerebral and Cardiovascular Center
- 3) Department of Preventive Cardiology, National Cerebral and Cardiovascular Center

Yu Matsumura<sup>1)</sup>, Aya Miyazaki<sup>1)</sup>, Heima Sakaguchi<sup>1)</sup>, Jun Negishi<sup>1)</sup>, Yoshihiro Miyamoto<sup>3)</sup>, Aiba Takeshi<sup>2)</sup>, Kengo Kusano<sup>2)</sup>, Shiraishi Isao<sup>1)</sup>, Ohuchi Hideo<sup>1)</sup>

# Background

## Genotype and Triggers for Life-Threatening events (cardiac arrest or SCD) in 110 LQTS patients



Schwartz et al, J Am Coll Cardiol. 2013 July 16; 62(3): 169–180

# Objectives

To evaluate the feature of type 3 congenital long QT syndrome (LQT3) who provoked Ventricular arrhythmia (VA) during exercise or crying

# Methods

Subjects: 4 patients with mutation of SCN5A

1. ECG { at rest  
during VA
2. Load test { Exercise stress  
Drug infusion
3. The locations of gene

## Epinephrine

After 0.1 $\mu$ g/kg bolus  
0.1 $\mu$ g/kg/min 5min

## Propranolol + Epinephrine

After 0.1mg/kg 5min  
0.1 $\mu$ g/kg/min 5min

## Mexiletine + Epinephrine

After 2.5mg/kg 5min  
0.1 $\mu$ g/kg/min 5min

Drug infusion protocol



# Patient Characteristics

	Case 1	Case 2	Case 3	Case 4
Age/Gender	8 y.o/M	17 y.o/M	15 y.o/M	15 y.o/F
Diagnosis time (Opportunity)	Neonatal (TdP)	Neonatal (TdP)	Neonatal (Family history)	12 y.o (School screening)
Trigger of VA (age)	Crying (neonatal)	Exercise (playing baseball)	Exercise (playing baseball)	Exercise (playing basketball)
Alive	Sudden death (at rest)	alive	alive (syncope during baseball)	alive

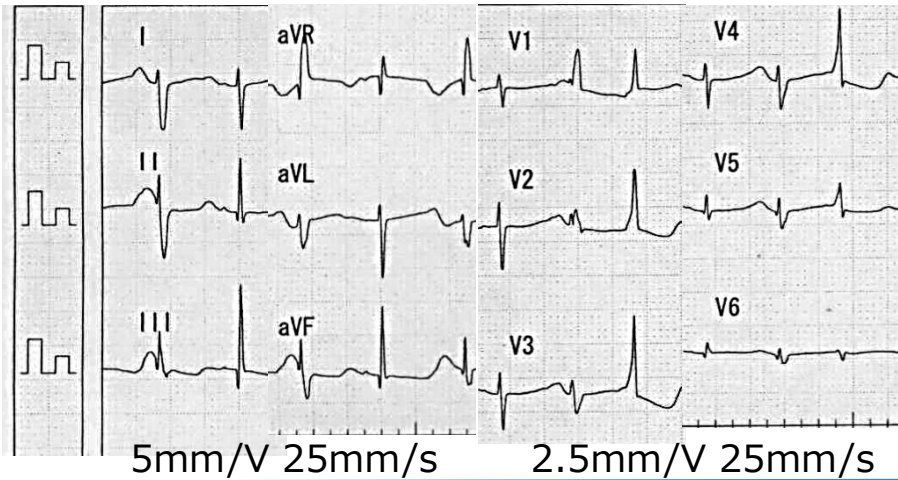


sibling

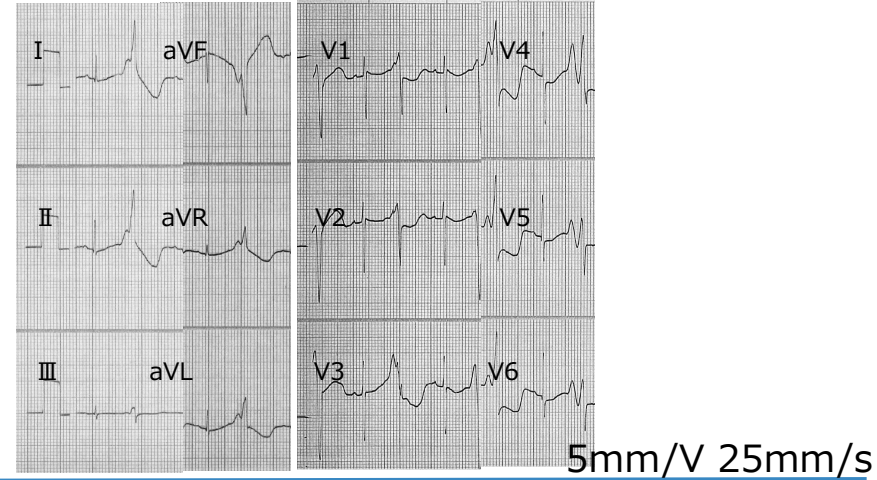
TdP : Torsade de Pointes  
VA : Ventricular Arrhythmia

# ECG at initial presentation

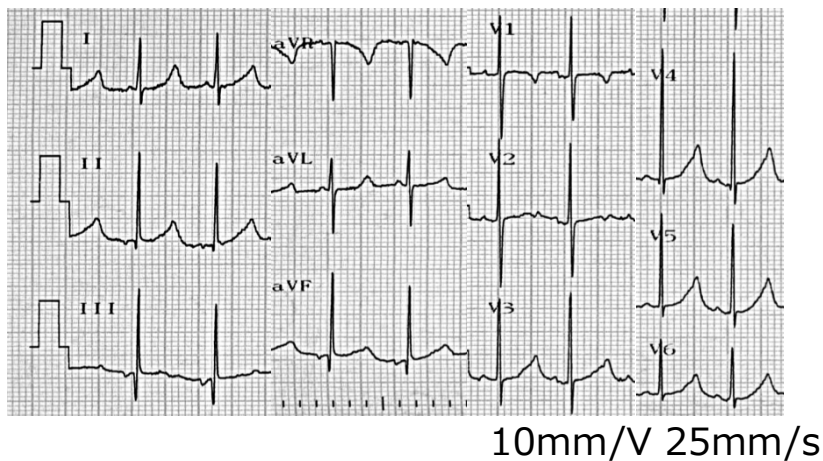
Case 1 (at birth) QTc=560 ms



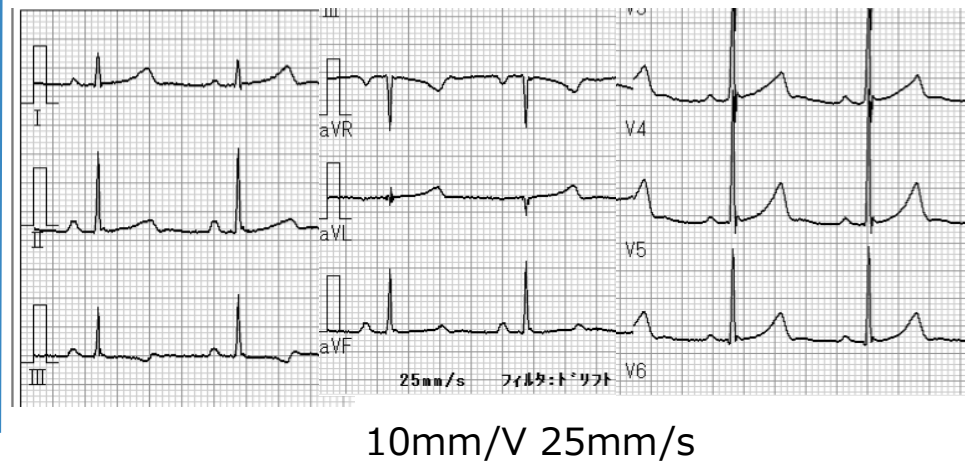
Case 2 (at birth) QTc (immeasurable)



Case 3 ( at 1 month) QTc=510 ms

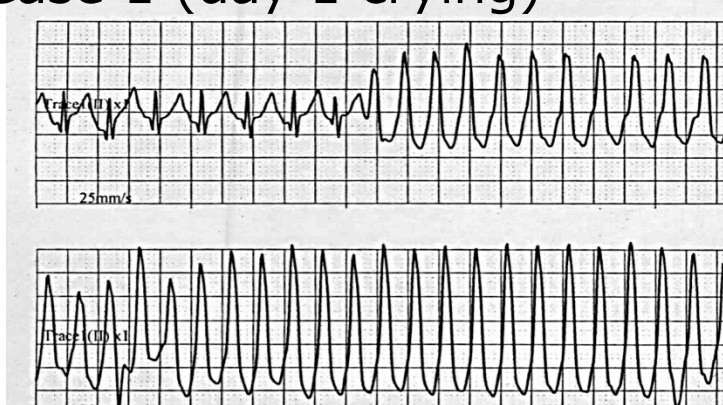


Case 4 (12 y.o) QTc=440 ms



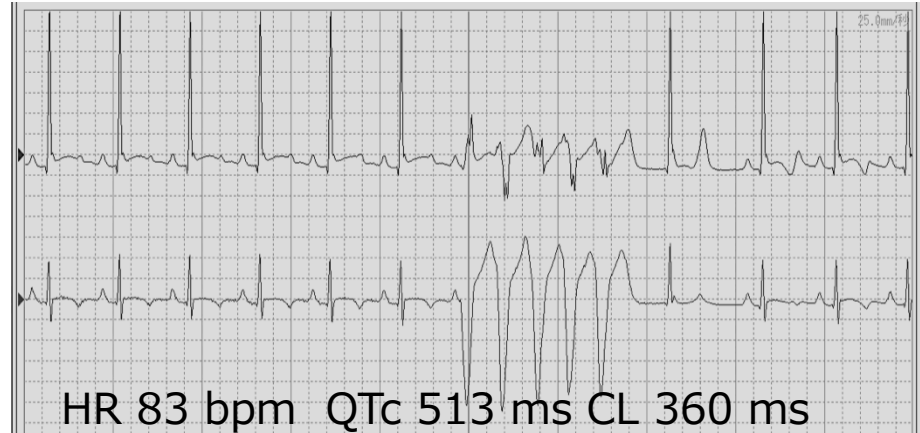
# ECG at VA

Case 1 (day 1 crying)



HR 210 bpm QTc 450 ms CL 188 ms

Case 2 (14 y.o during baseball)



HR 83 bpm QTc 513 ms CL 360 ms

Case 3 (13 y.o during baseball)



HR 141 bpm QTc 456 ms CL 240 ms

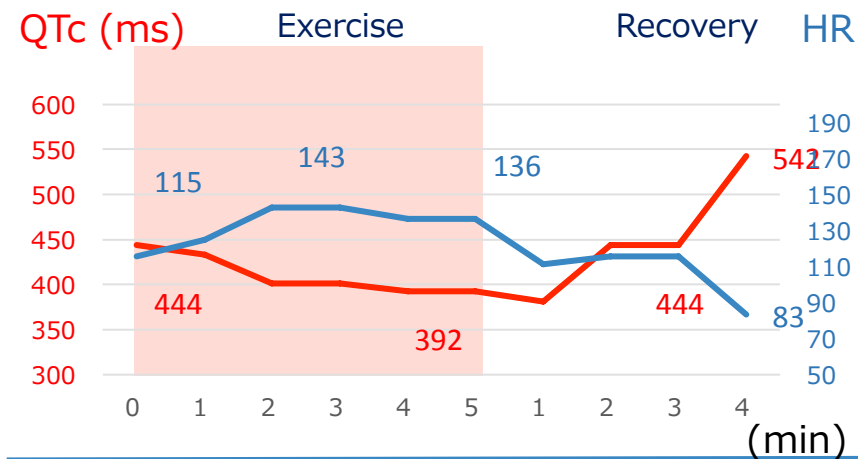
Case 4 (12 y.o during basketball)



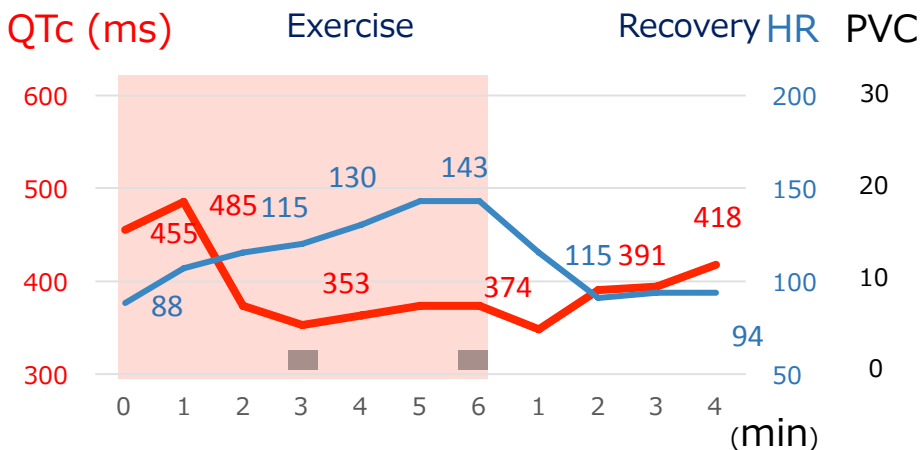
HR 174 bpm QTc 450 ms CL 220 ms

# Exercise Stress Test

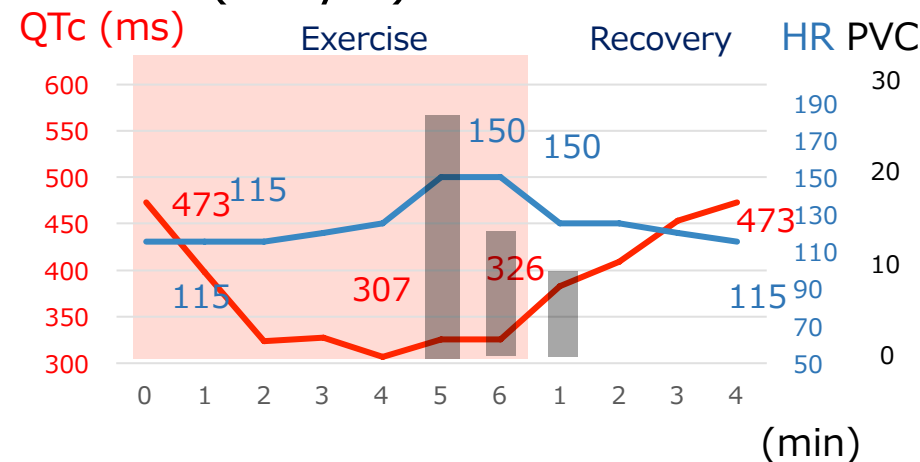
Case 1 (6 y.o under  $\beta$ blocker)



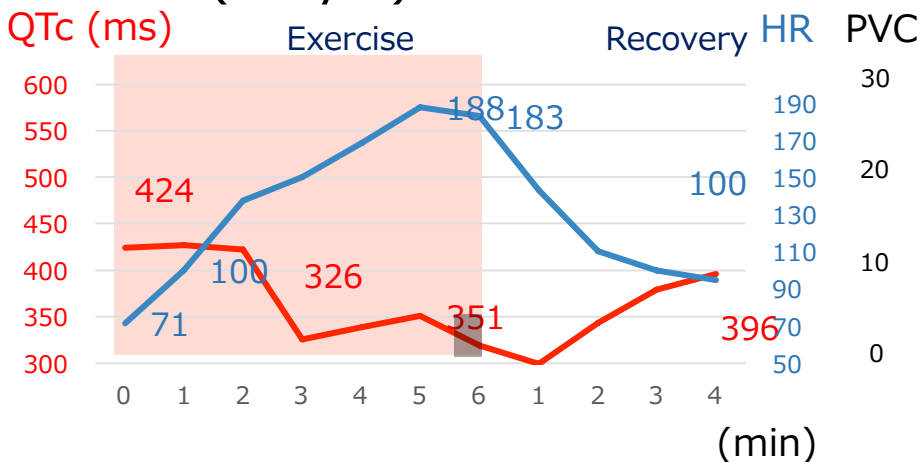
Case 2 (14 y.o under  $\beta$ blocker)



Case 3 (13 y.o)

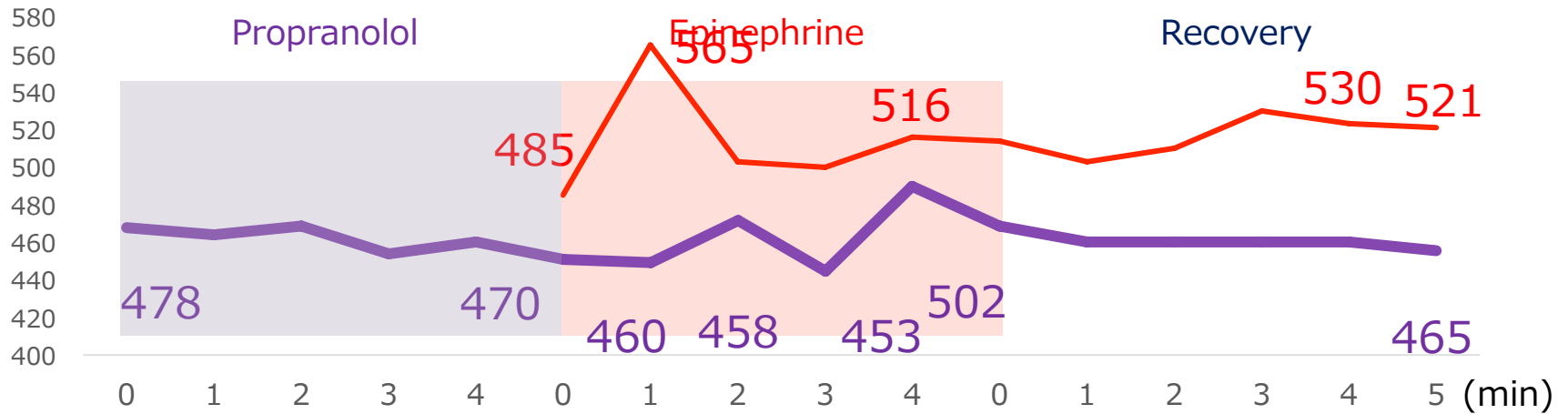


Case 4 (12 y.o)

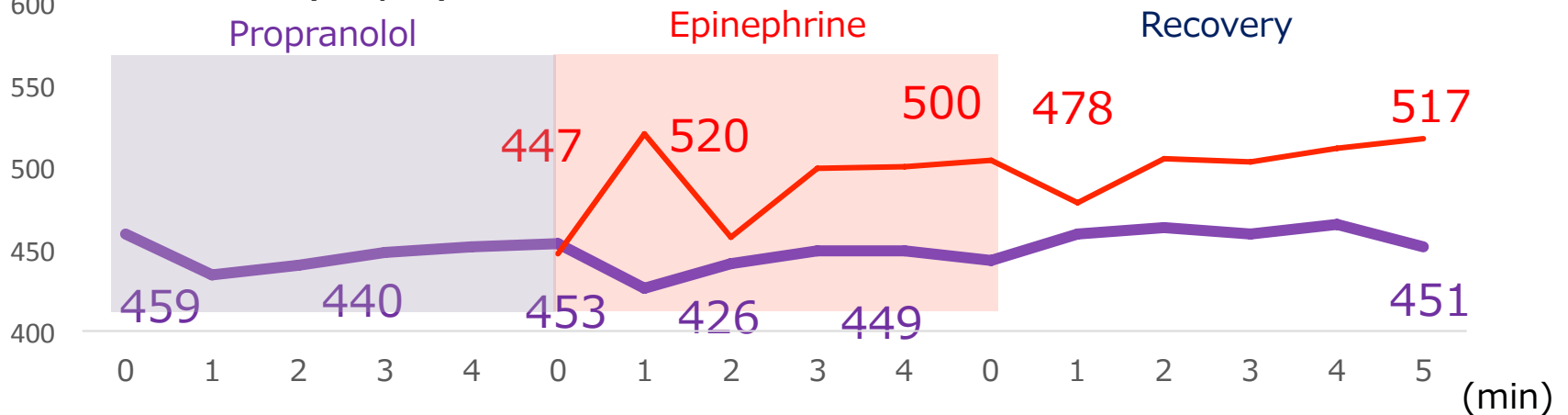


# Drug infusion test (Epi+Prop)

QTc (ms) Case 3 (13y.o)

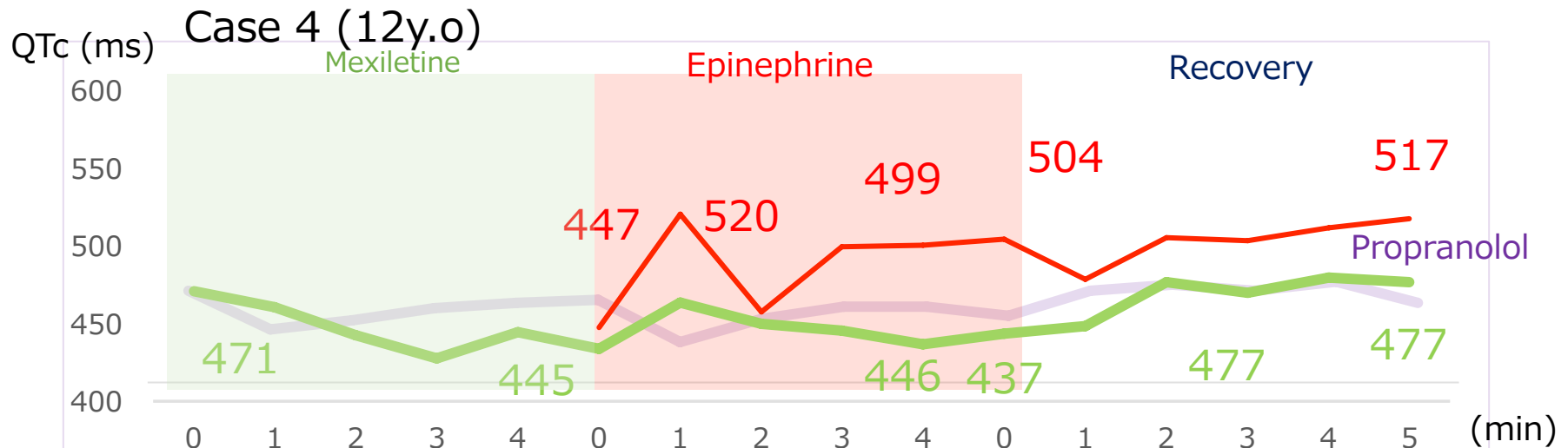
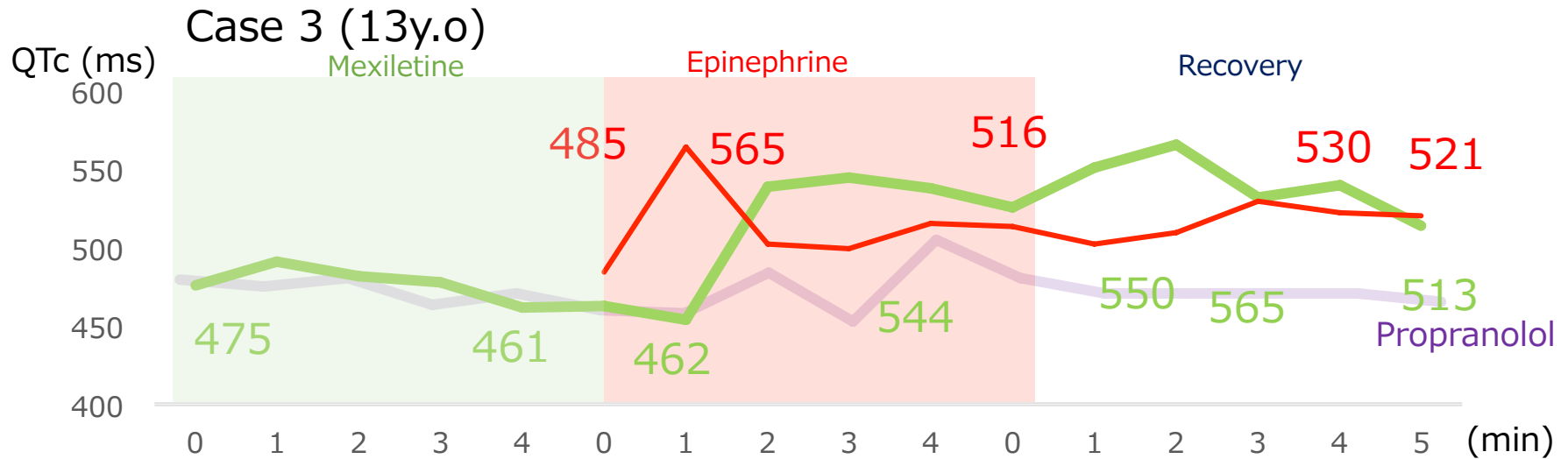


QTc (ms) Case 4 (12y.o)



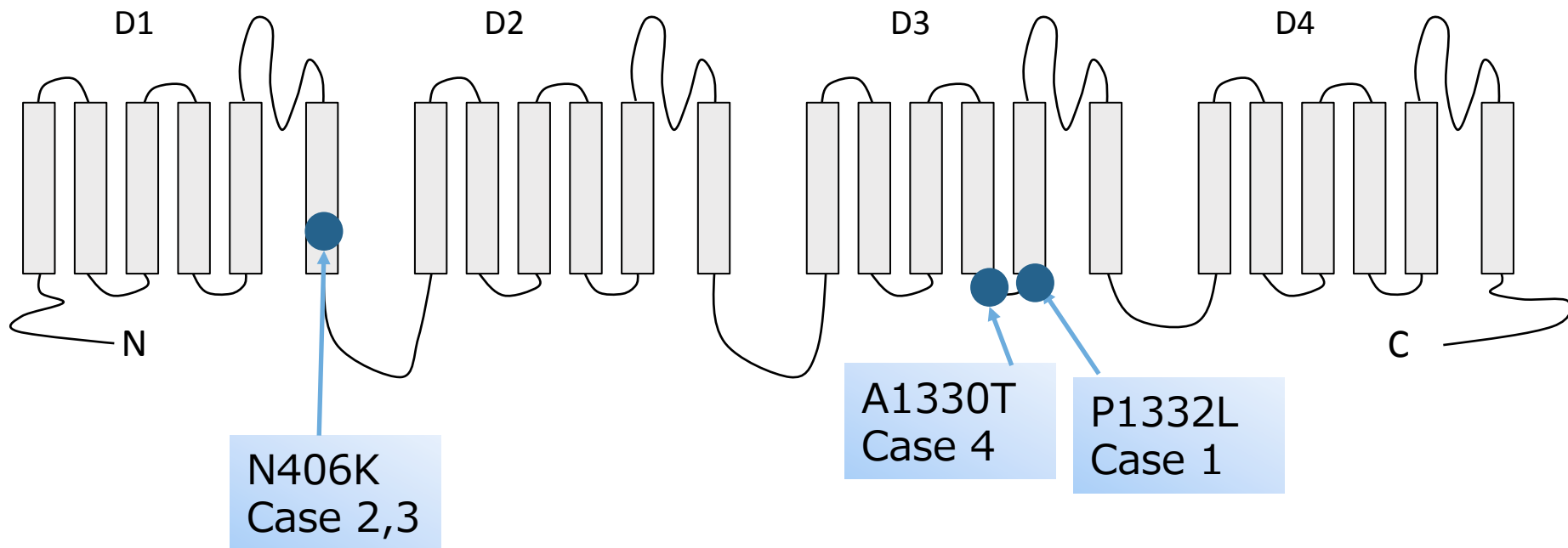


# Drug infusion test (Epi+Mex)



# Locations of genetic mutation

The Nav1.5 cardiac sodium channel  $\alpha$ -subunit (SCN5A)

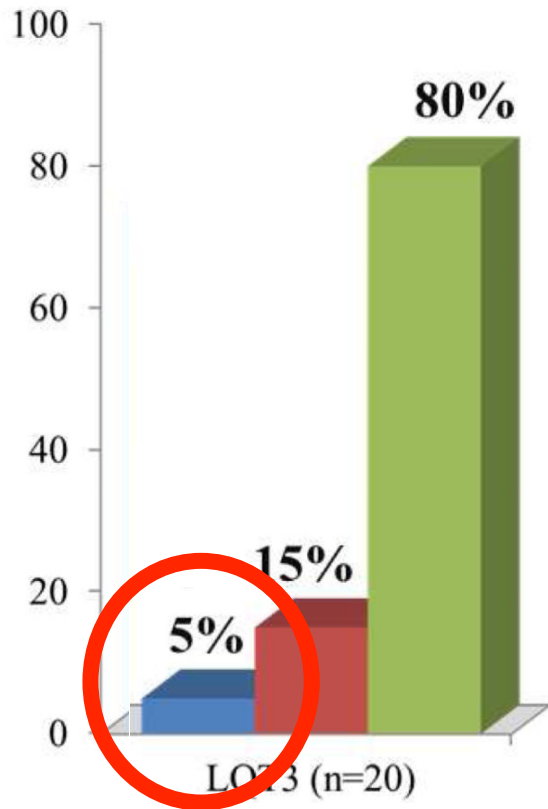


	Case 1	Case 2	Case 3	Case 4
Age/Gender	8y.o/M	17y.o/M	15y.o/M	15y.o/F
Diagnosis time (Opportunity)	Neonatal (TdP)	Neonatal (TdP)	Neonatal (Family history)	12y.o (School screening)
Trigger of VA	Crying (neonatal)	Exercise (playing baseball)	Exercise (playing baseball)	Exercise (playing basketball)
Exercise Stress Test	QTc ↓	QTc ↓	QTc ↓	QTc ↓
Drug infusion test	N/A	N/A	Epi QTc ↑ Prop QTc ↓ Mex QTc ↑	Epi QTc ↑ Prop QTc ↓ Mex QTc ↓
alive	Sudden death (at rest)	alive	alive (syncope during baseball)	alive

# Discussion

Why did these 4 cases provoke VA during exercise?

# Discussion



80% of LQT3 patients show cardiac event at **REST**

LESS likely to be triggered by adrenergic stress

■ Exercise ■ Emotion ■ Sleep, rest without arousal

Schwartz et al, J Am Coll Cardiol. 2013 July 16; 62(3): 169–180



# Discussion

	Case 1	Case 2	Case 3	Case 4
Exercise Stress test	QTc ↓	QTc ↓	QTc ↓	QTc ↓
Drug Infusion test	N/A	N/A	Epi QTc ↑ Prop QTc ↓ Mex QTc ↑	Epi QTc ↑ Prop QTc ↓ Mex QTc ↓

What makes difference??

All cases shortened QTc during exercise

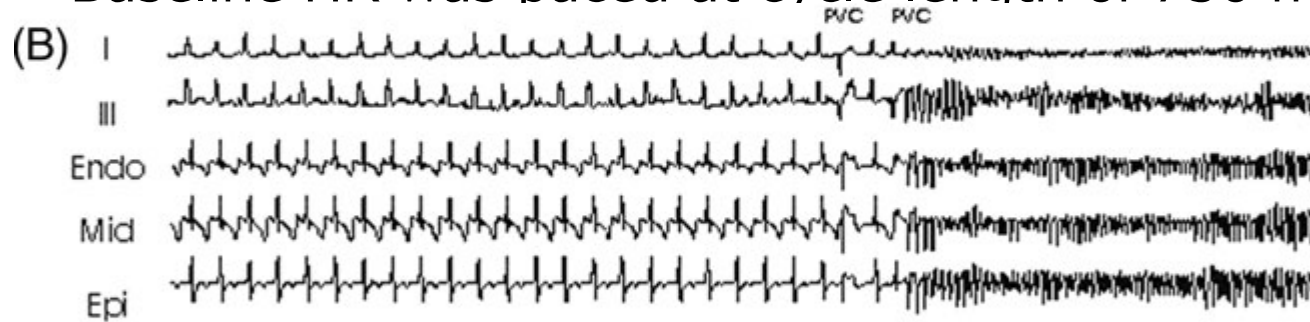
Two patients who performed drug infusion test prolonged QTc during epinephrine infusion

# Discussion

## Adrenergic stimulation by epinephrine



Baseline HR was paced at cycle length of 750 ms

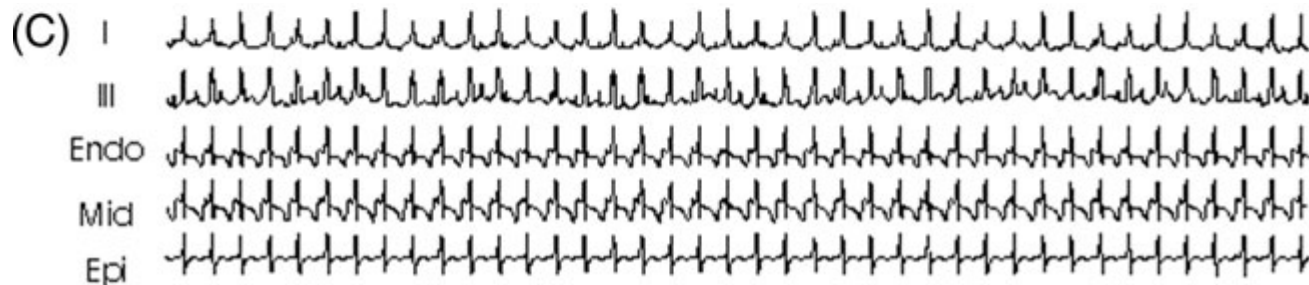


0.5 $\mu$ g/kg of epinephrine induced neither PVC nor VA  
Administered in a dose of 1.0  $\mu$ g/kg of epinephrine  
PVCs were provoked and polymorphic VA induced.

Chinushi et al, Europace (2008) 10, 249–255

# Discussion

## Adrenergic stimulation by epinephrine



After administration of propranolol

Administered in a dose of 1.0  $\mu\text{g}/\text{kg}$  of epinephrine

Neither PVC nor VA were shown

# Discussion

This study shows

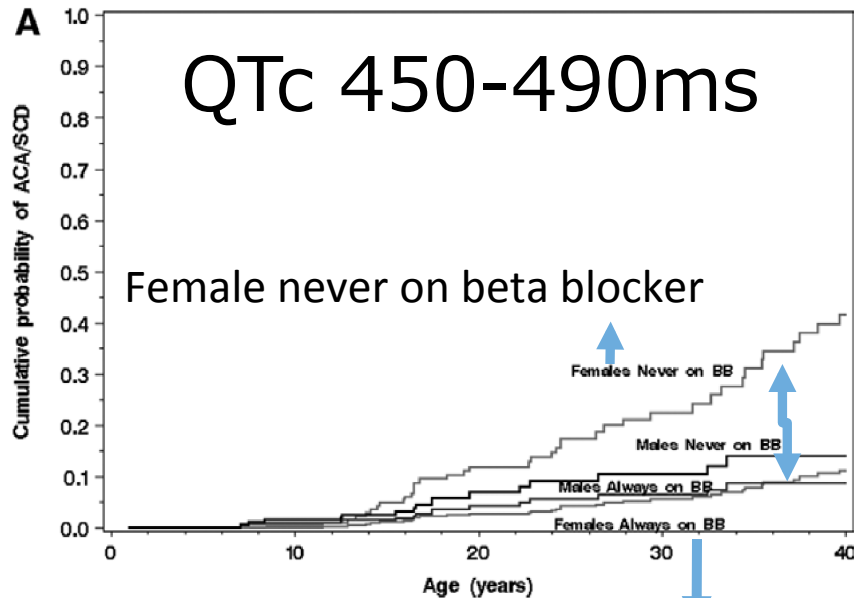
In LQT3 model dogs,  
Pro-arrhythmic effect of epinephrine depending on  
the intensity of adrenergic stimulation.

Beta blocker suppressed epinephrine-induced arrhythmia.

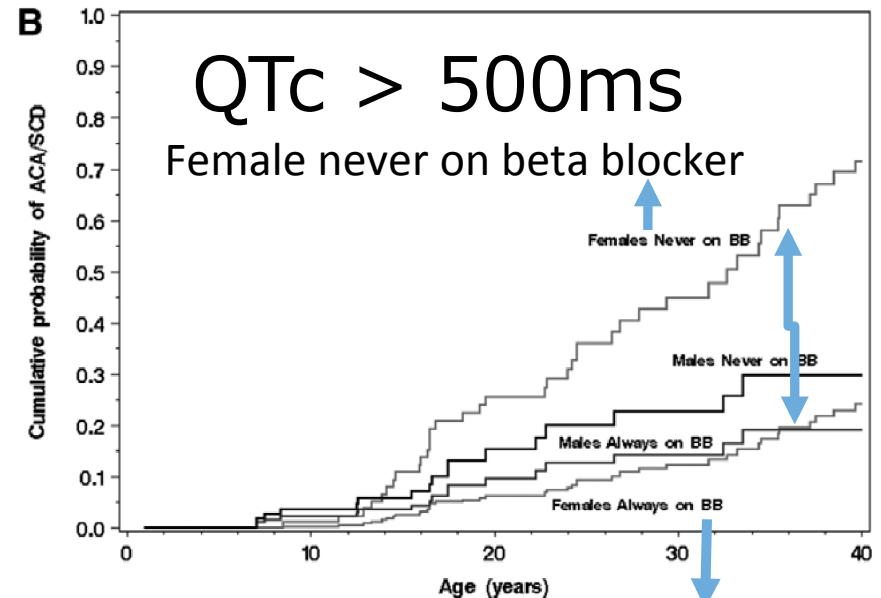
Chinushi et al, Europace (2008) 10, 249–255

# Discussion

## Effect of beta blocker in LQT3 patients



Female always on beta blocker



Female always on beta blocker

Beta blocker therapy was associated with an 83% reduction in cardiac events in female.



# Summary

We showed four LQT3 patients which exhibited VA during exercise or crying.

The Holter monitoring during intensive exercise and epinephrine test were more useful to determine cardiac event or the QT prolongation than the exercise stress test.

We speculated that these findings might be effected by the intensity of adrenergic stimulation .

# Conclusion

Even in LQT3, the adrenergic activity can be the trigger of cardiac events.