

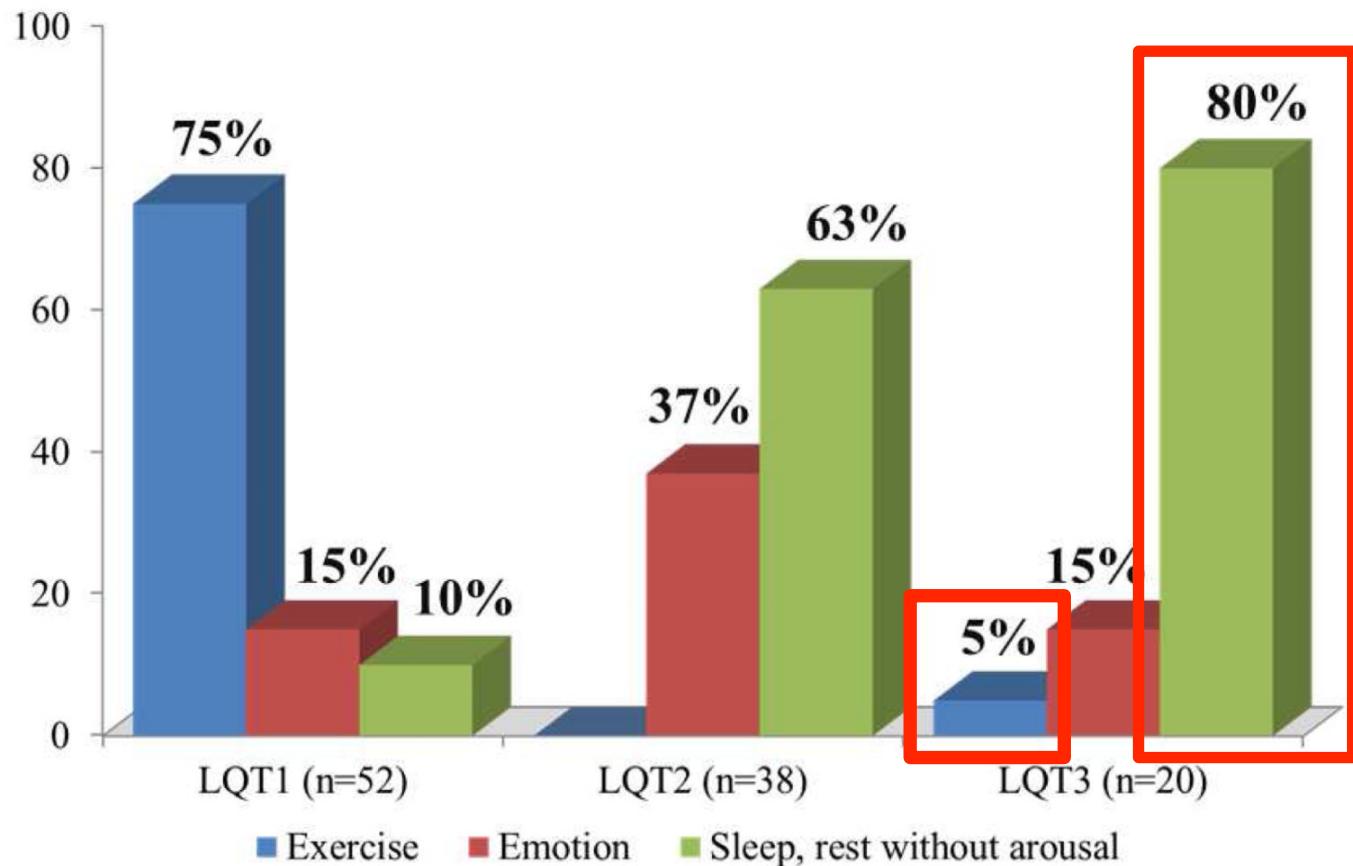
Ventricular tachyarrhythmia provoked by exercise in pediatric patients with type 3 congenital long QT syndrome

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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 s...
Drug infus...

3. The locations of gene

Epinephrine

After 0.1 μ g/kg bolus
0.1 μ g/kg/min 5min

Propranolol + Epinephrine

After 0.1mg/kg 5min
0.1 μ g/kg/min 5min

Mexiletine + Epinephrine

After 2.5mg/kg 5min
0.1 μ g/kg/min 5min

Drug infusion protocol

Shimizu W et al, Heart Rhythm, 2004;1:276-282

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

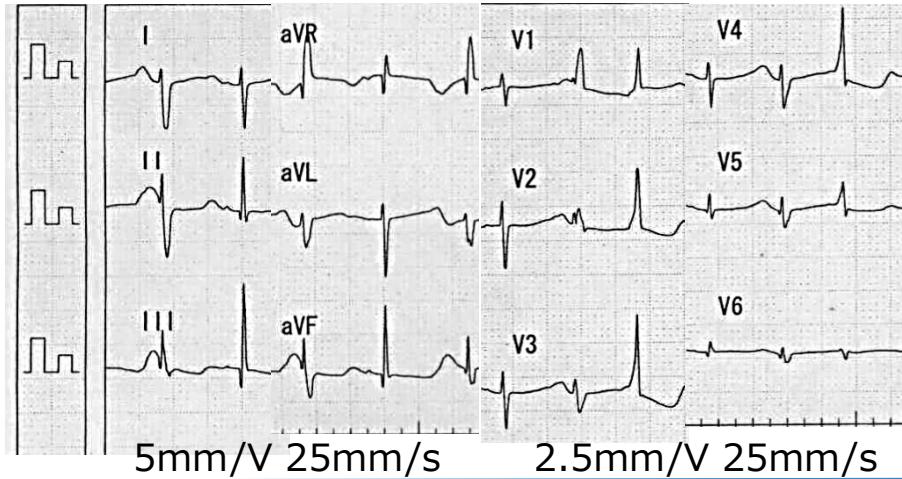
TdP
VA

: Torsade de Pointes
: Ventricular Arrhythmia

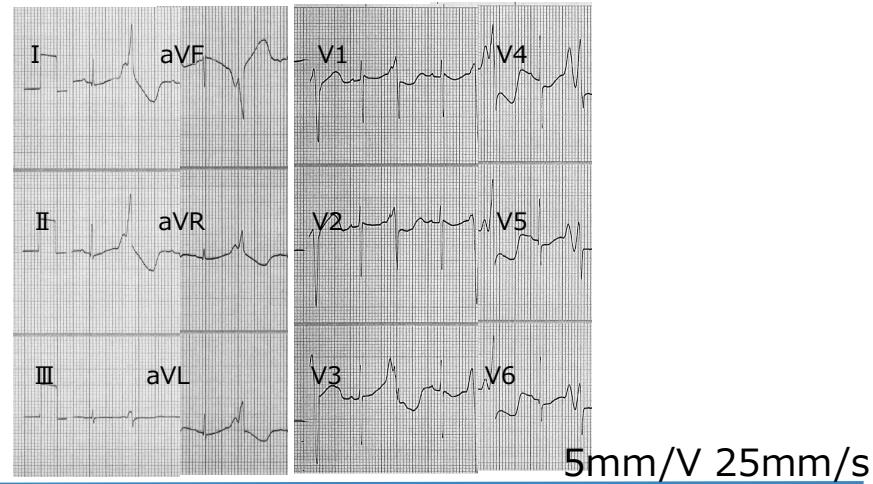
sibling

ECG at initial presentation

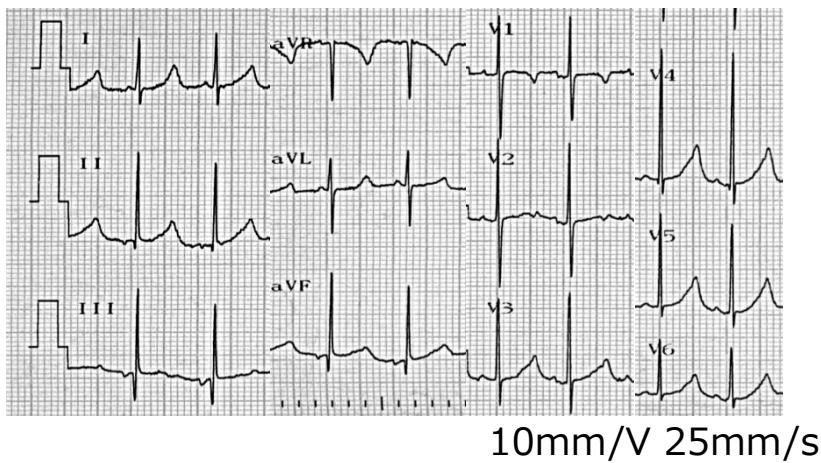
Case 1 (at birth) QTc=560 ms



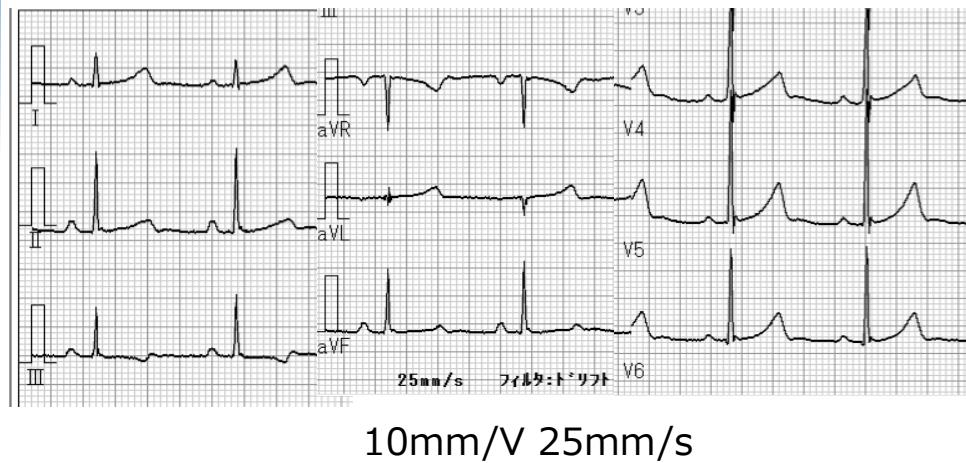
Case 2 (at birth) QTc (immeasurable)



Case 3 (at 1 month) QTc=510 ms

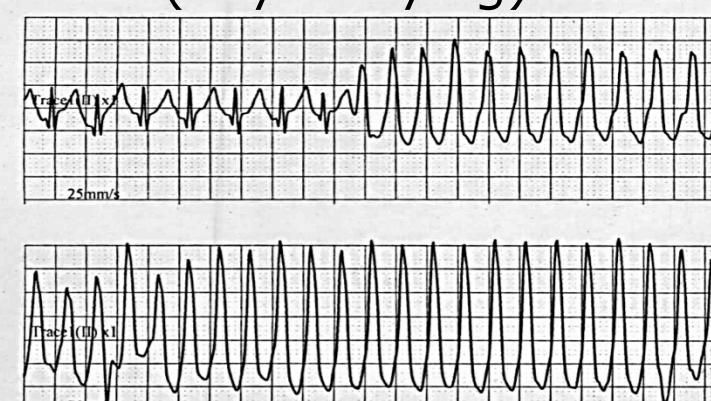


Case 4 (12 y.o) QTc=440 ms



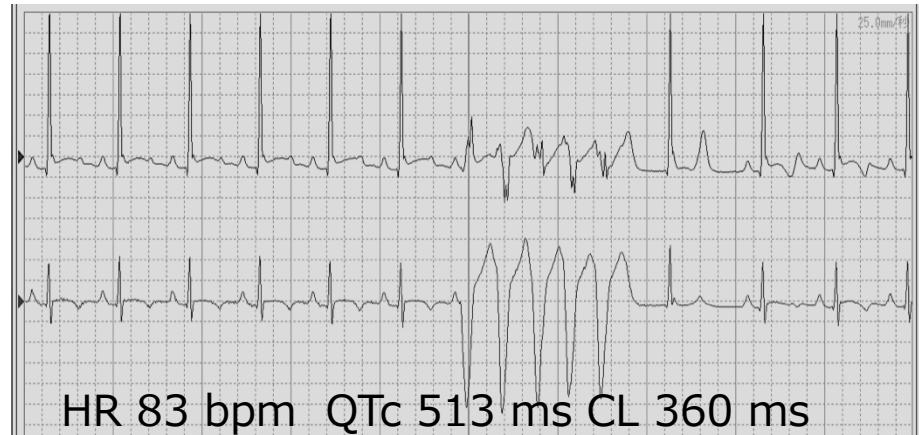
ECG at VA

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

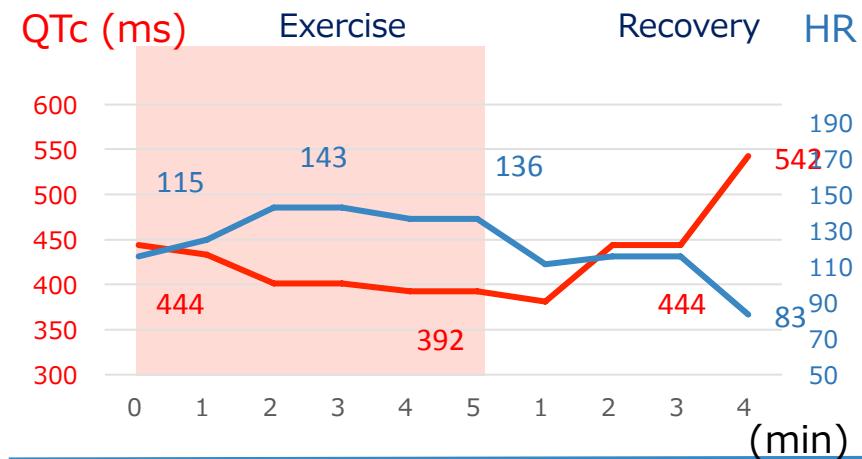
Case 4 (12 y.o during basketball)



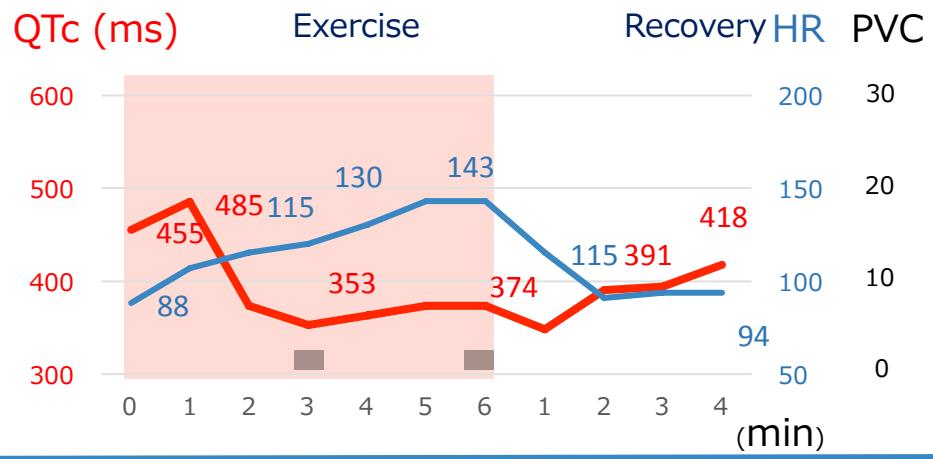
HR 174 bpm QTc 450 ms CL 220 ms

Exercise Stress Test

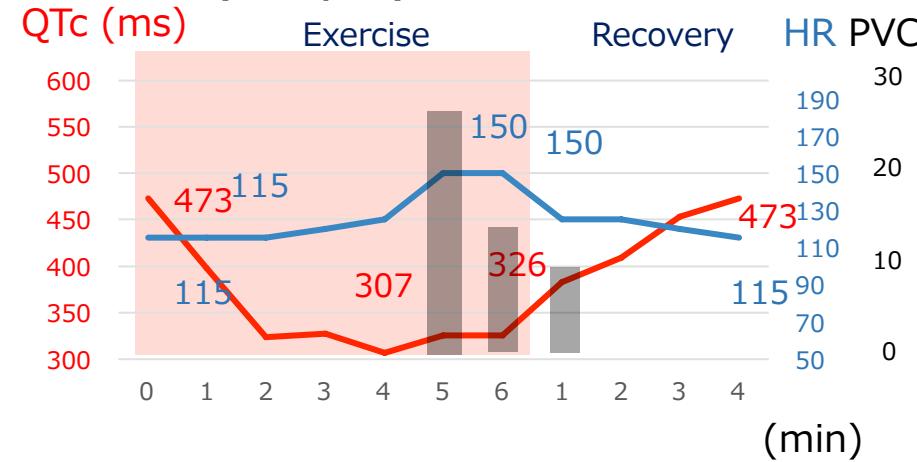
Case 1 (6 y.o under β blocker)



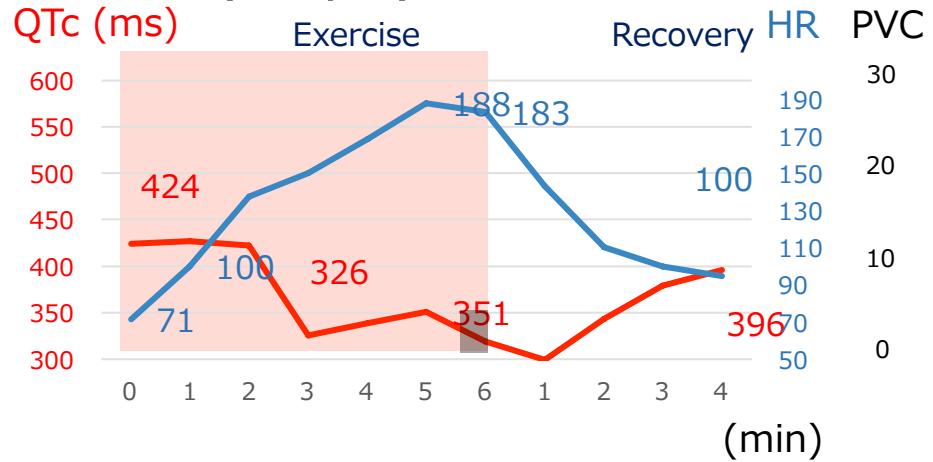
Case 2 (14 y.o under β blocker)



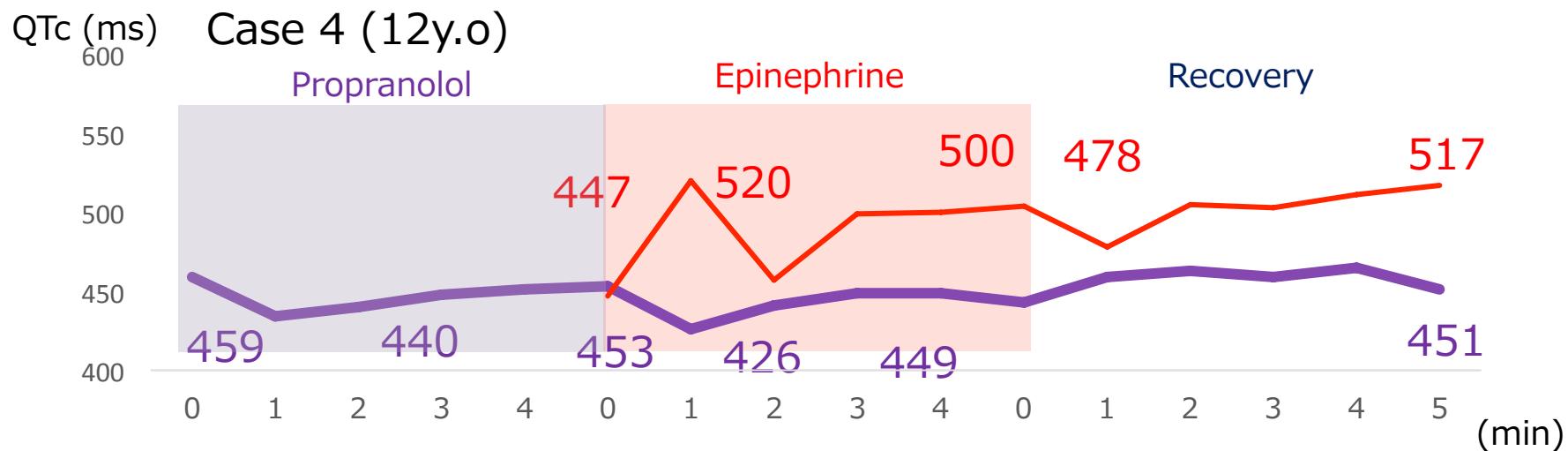
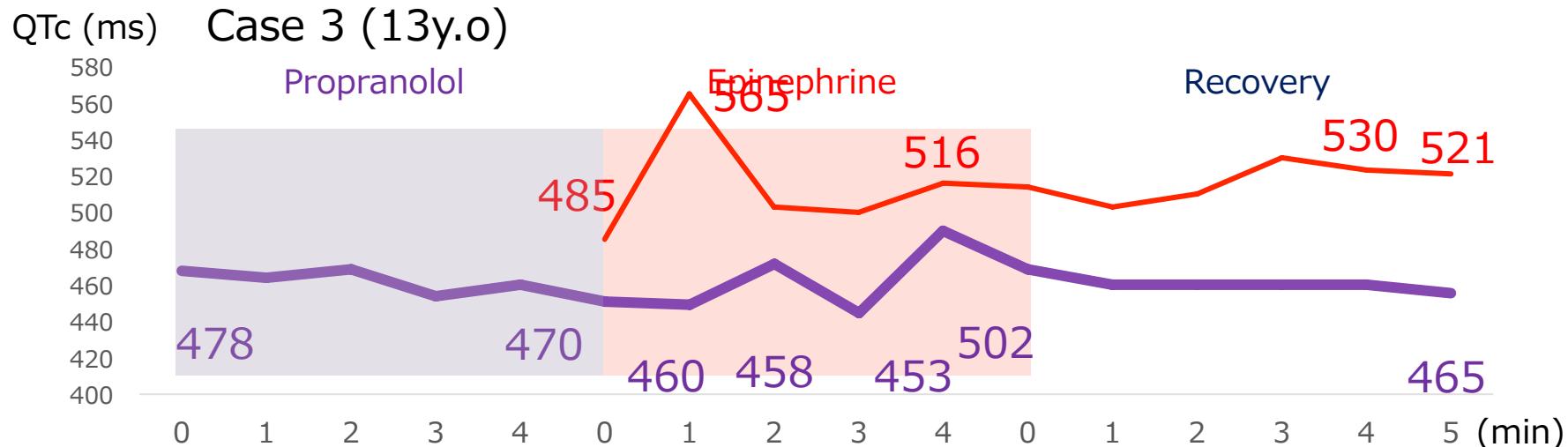
Case 3 (13 y.o)



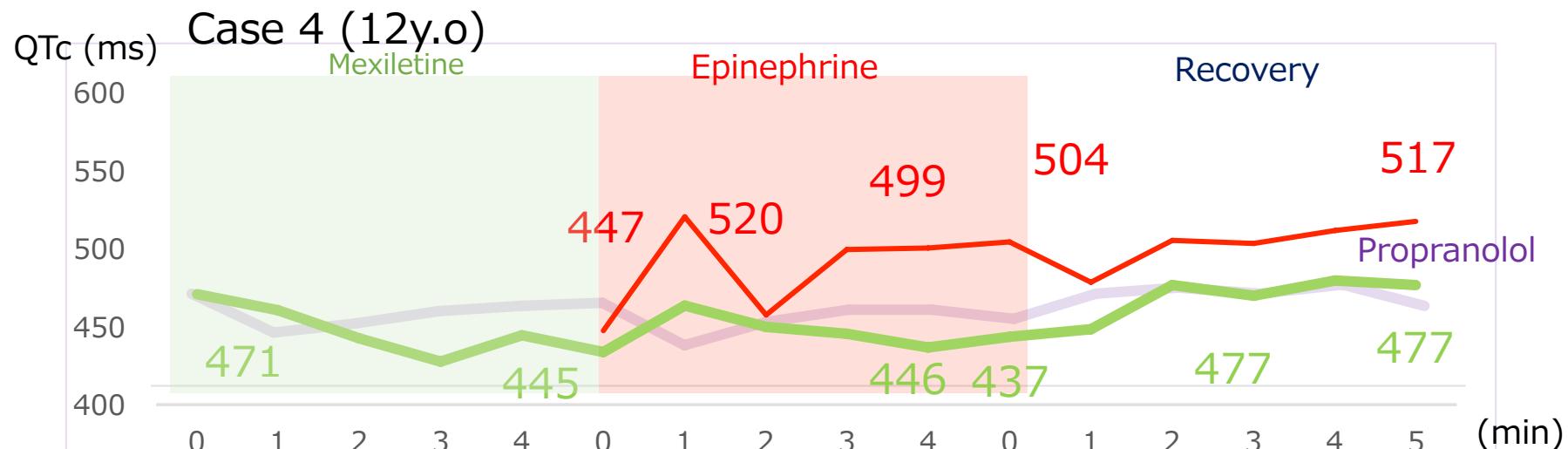
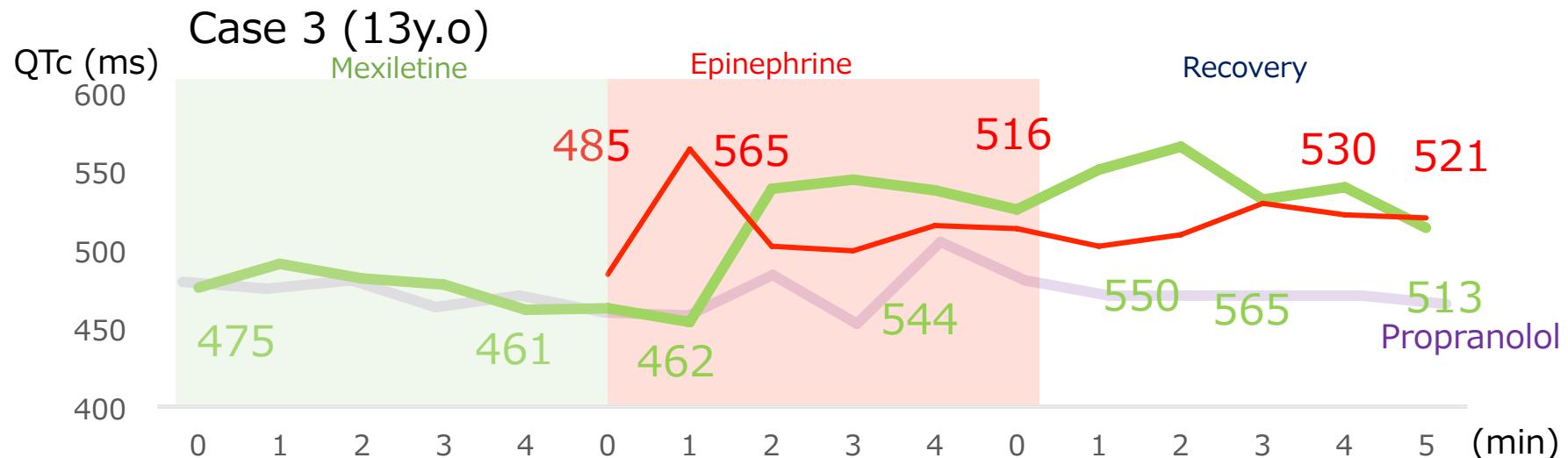
Case 4 (12 y.o)



Drug infusion test (Epi+Prop)

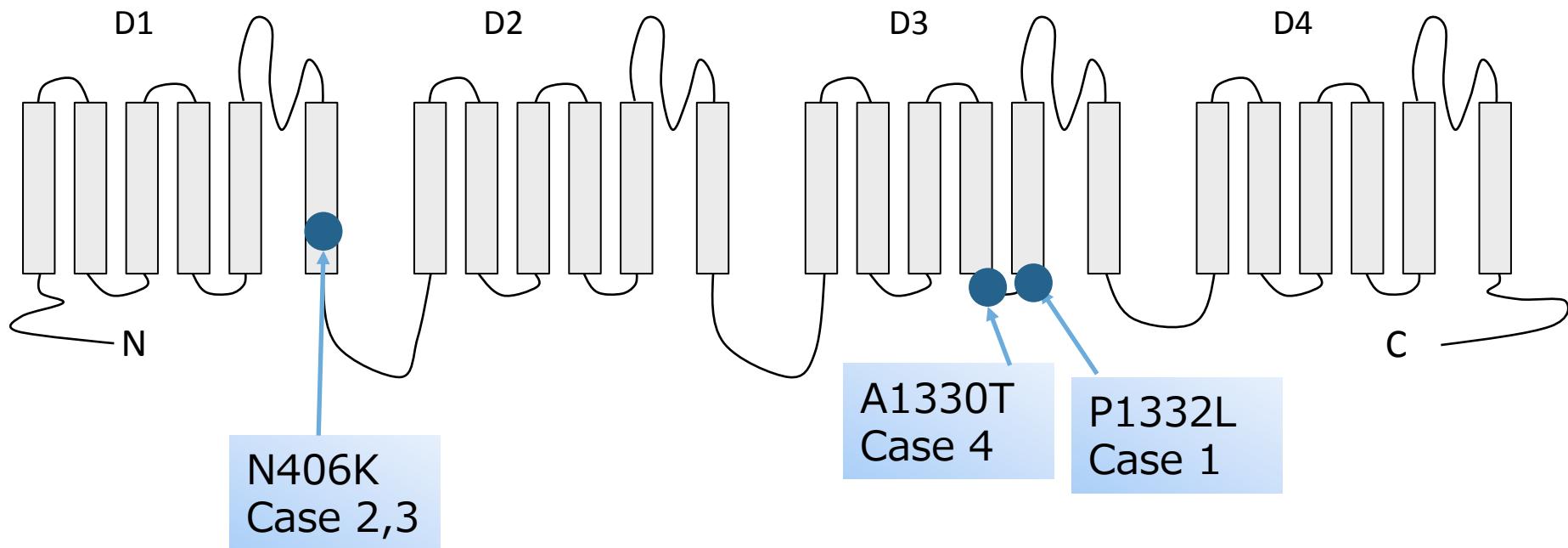


Drug infusion test (Epi+Mex)



Locations of genetic mutation

The Nav1.5 cardiac sodium channel α -subunit (SCN5A)

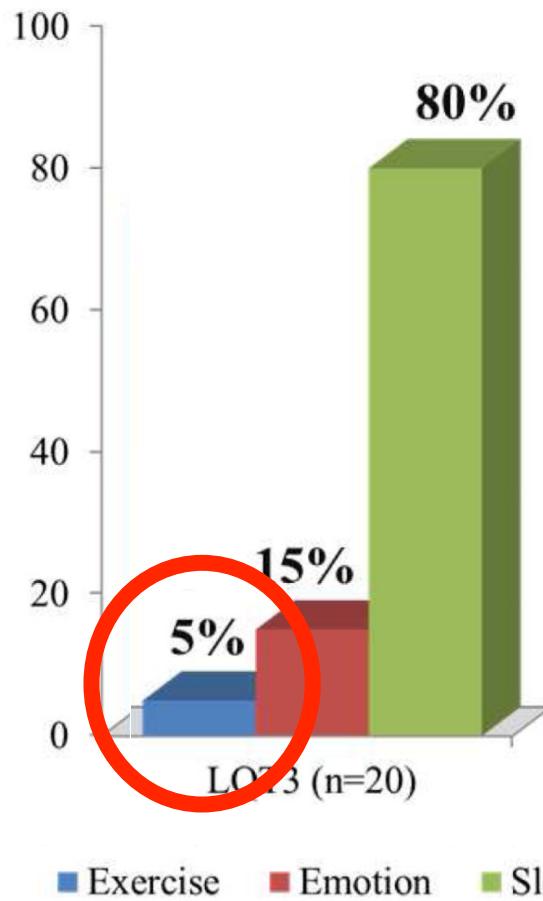


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Trigger of VA	Crying (neonatal)	Exercise (playing baseball)	Exercise (playing baseball)	Exercise (playing basketball)
Exercise Stress Test	QTc ↓	QTc ↓	QTc ↓	QTc ↓
Drug infusion test	N/A	N/A	Epi QTc ↑ Prop QTc ↓ Mex QTc ↑	Epi QTc ↑ Prop QTc ↓ Mex QTc ↓
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

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??

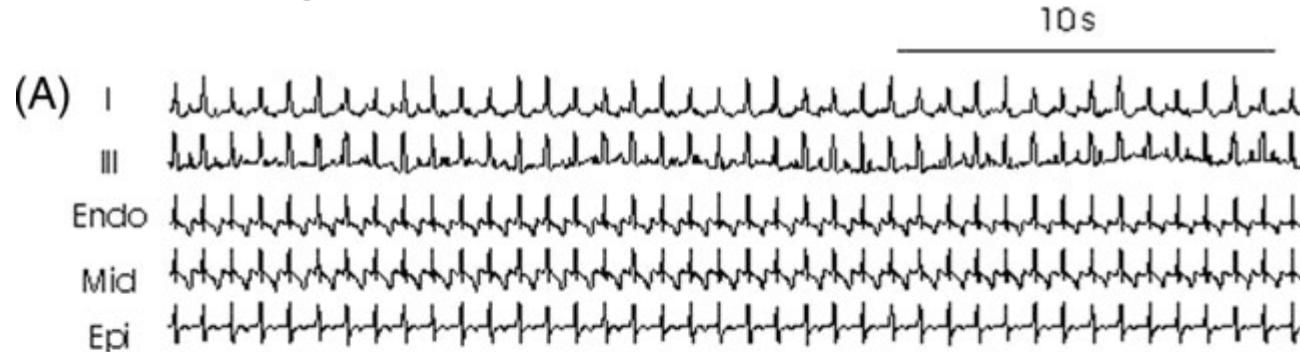
All cases shortened QTc during exercise



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

Discussion

Adrenergic stimulation by epinephrine

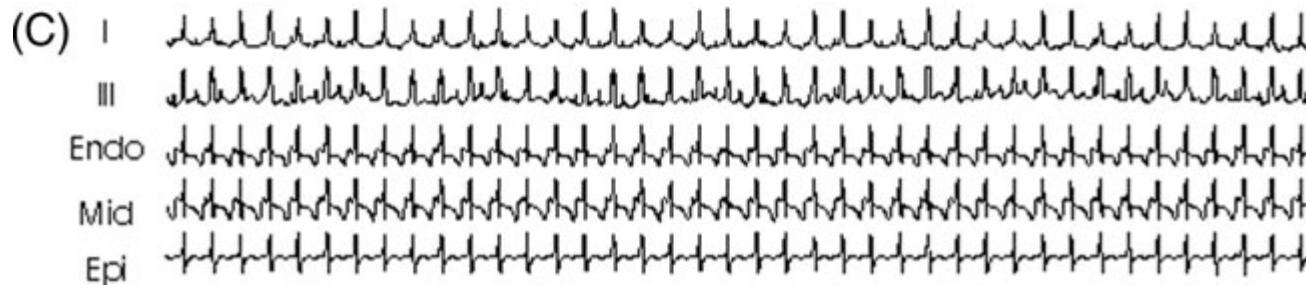


0.5 μ g/kg of epinephrine induced neither PVC nor VA
Administered in a dose of 1.0 μ g/kg of epinephrine
PVCs were provoked and polymorphic VA induced.

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

Discussion

Adrenergic stimulation by epinephrine



After administration of propranolol
Administered in a dose of 1.0 µg/kg of epinephrine

Neither PVC nor VA were shown

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

Discussion

This study shows

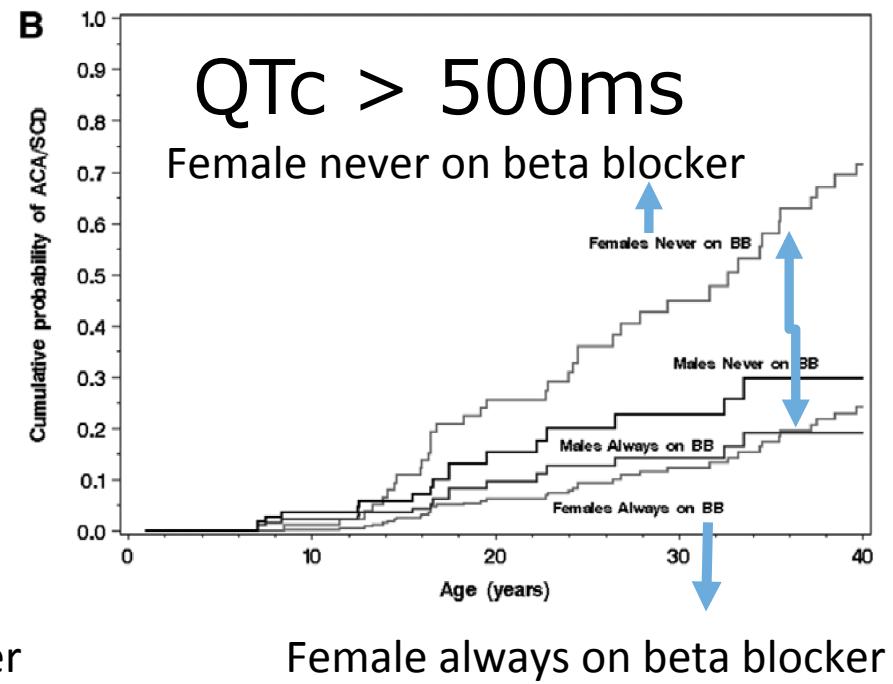
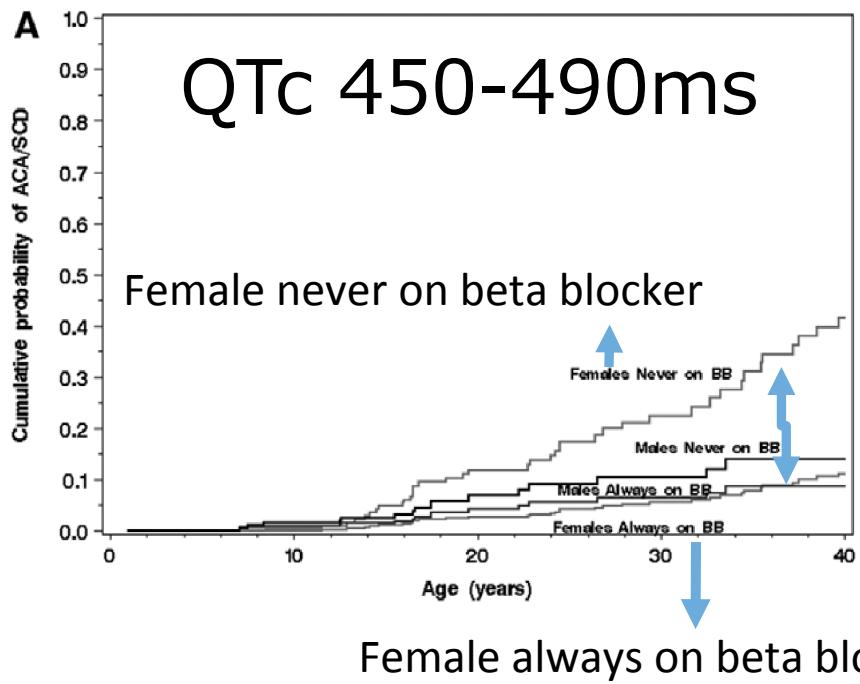
In LQT3 model dogs,
Pro-arrhythmic effect of epinephrine depending on
the intensity of adrenergic stimulation.

Beta blocker suppressed epinephrine-induced arrhythmia.

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

Discussion

Effect of beta blocker in LQT3 patients



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.