Na

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KAKIMURA Jun-ichi Functional roles of voltage gated Na^+ channels in pain sensation.

Quality of life

(QOL)

(NSAIDs)

(dorsal root ganglion, DRG)

Aβ ,Aδ ,C

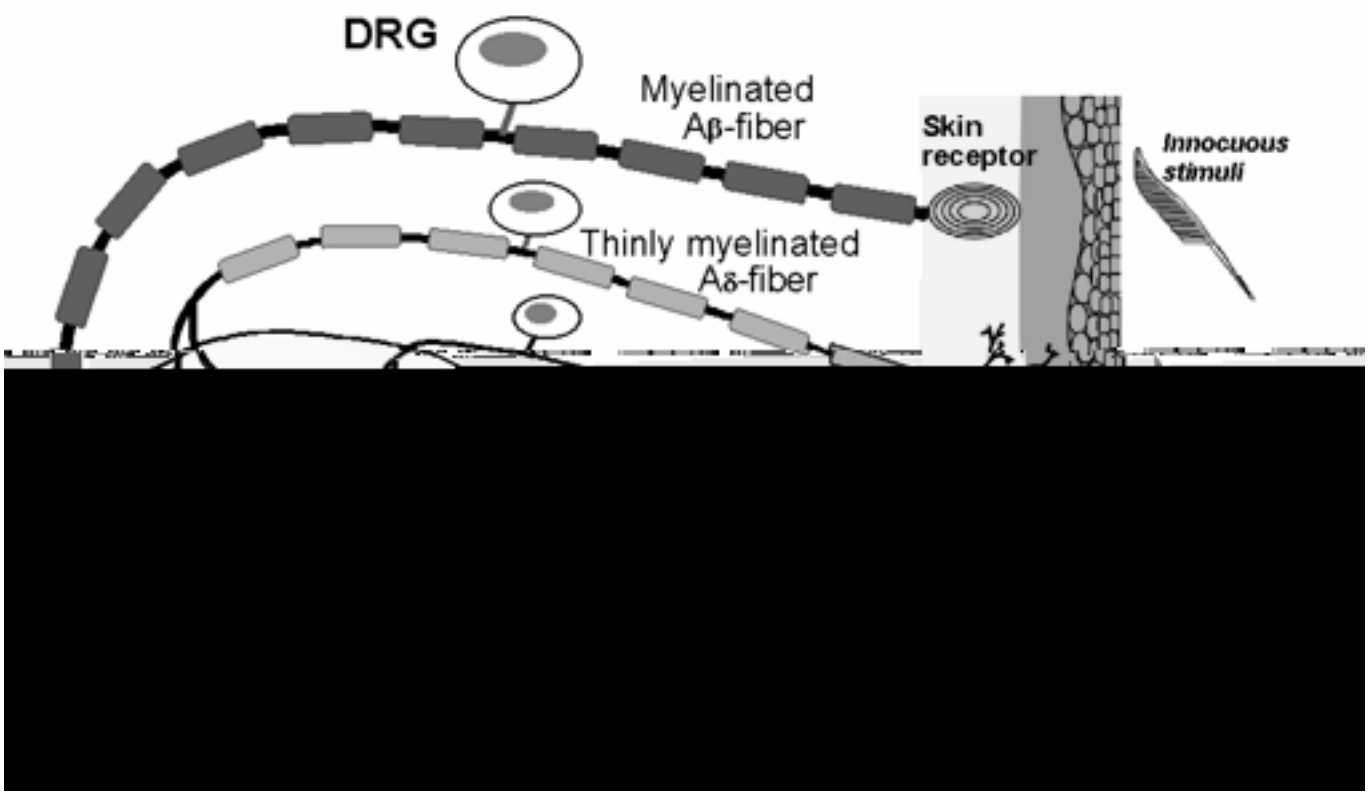
,

Aβ

Aδ

C Aδ

C



1

C [1), 2)] 1 Na

2A

2B

Na Na m

Na h resting state

m Na

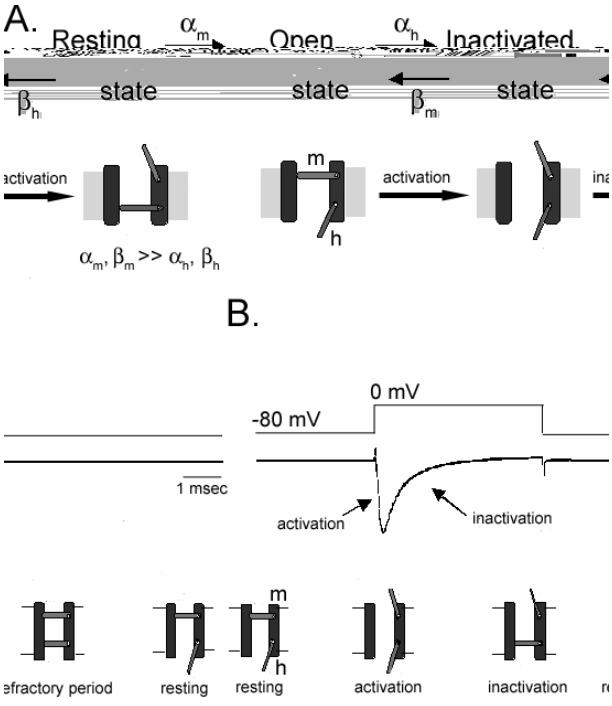
m

Na Na

Na h Na

m h

Na m



2 Na A

B Na

h m

Na

refractory period

h

repriming

Na

⇔ ⇔

Na

Na 3), 4)

Na

α 260 kDa

β α

$Na_V1.1$ $Na_V1.9$

9 1

50

3), 5), 6)

Na

TTX

TTX Na TTX

TTX Na

DRG TTX Na

$Na_V1.6$, $Na_V1.7$

TTX Na $Na_V1.8$,

$Na_V1.9$ C

7),8), 9),10)

$Na_V1.8$

10)

$Na_V1.8$ mRNA

TTX Na 11)

$Na_V1.9$

DRG

8) $Na_V1.9$ GDNF

$Na_V1.9$

GDNF

12), 13)

GDNF

$Na_V1.9$ mRNA

14)

		TTX	DRG	
$Na_V1.1$	*SCN1A*	nM	+	( )
$Na_V1.2$	*SCN2A*	nM	+	( )
$Na_V1.3$	*SCN3A*	nM		( )
$Na_V1.4$	*SCN4A*	nM	+	( )
$Na_V1.5$	*SCN5A*	μM	+	( )
$Na_V1.6$	*SCN8A*	nM	+	( )
$Na_V1.7$	*SCN9A*	nM	+	( )
$Na_V1.8$	*SCN10A*		+	( )
$Na_V1.9$	*SCN11A*		+	( )

1 Na α

Na

$Na_V1.8$, $Na_V1.9$ Aδ C

TTX Na

$Na_V1.9$

DRG Na

$Na_V1.9$

DRG $Na_V1.8$, $Na_V1.9$ 2

TTX Na

$Na_V1.9$

$Na_V1.8$-KO [10] DRG

30 μm

V_h

-80mV 200 V_t

Na

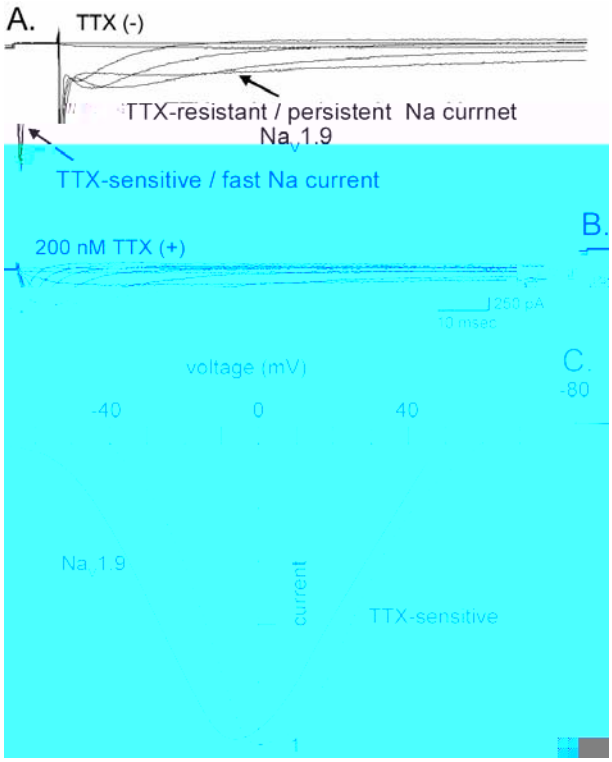
TTX

4A

200 nM TTX

4B $Na_V1.9$

1999 [17]



4 $Na_V1.8$-KO DRG Na

A TTX Na B 200 nM TTX

Na C $Na_V1.9$ -

$Na_V1.9$ Na

-60 mV

Na -40 mV

-20 mV

V_t = -20

mV 4C

h

steady-state activation curve m_∞ curve

steady-state inactivation curve h_∞ curve

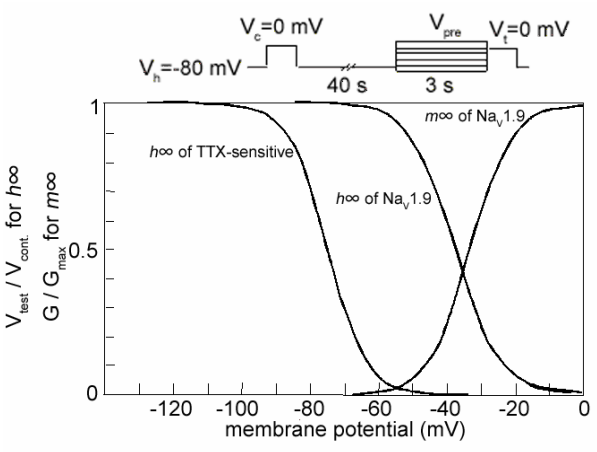
m_∞ curve $V_{1/2}$ = -31.5 ± 1.4 mV h_∞ curve

$V_{1/2}$ = -42.3 ± 1.7 mV h_∞ curve $V_{1/2}$

Na

$Na_V1.9$ Na

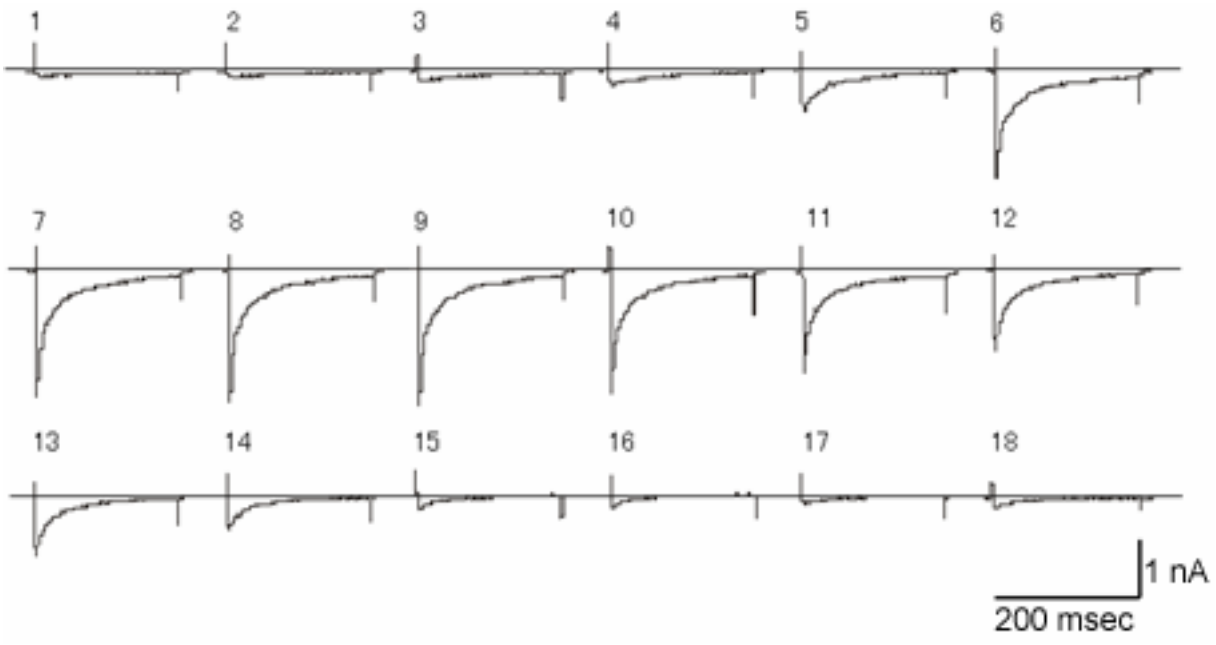
5



5 $Na_V1.9$ h_∞ curve m_∞ curve TTX

Na h_∞ curve h_∞

$Na_V1.9$



6 $Na_V1.9$ 30 (1→18)

PKA PKC

21)

washout $Na_V1.8$

washout ATP

run-down $Na_V1.9$

$Na_V1.9$

ATP

ATP V_h = -80 mV 30 V_t =

-20 mV $Na_V1.9$

18), 19)

6 $Na_V1.9$

10

A PKA

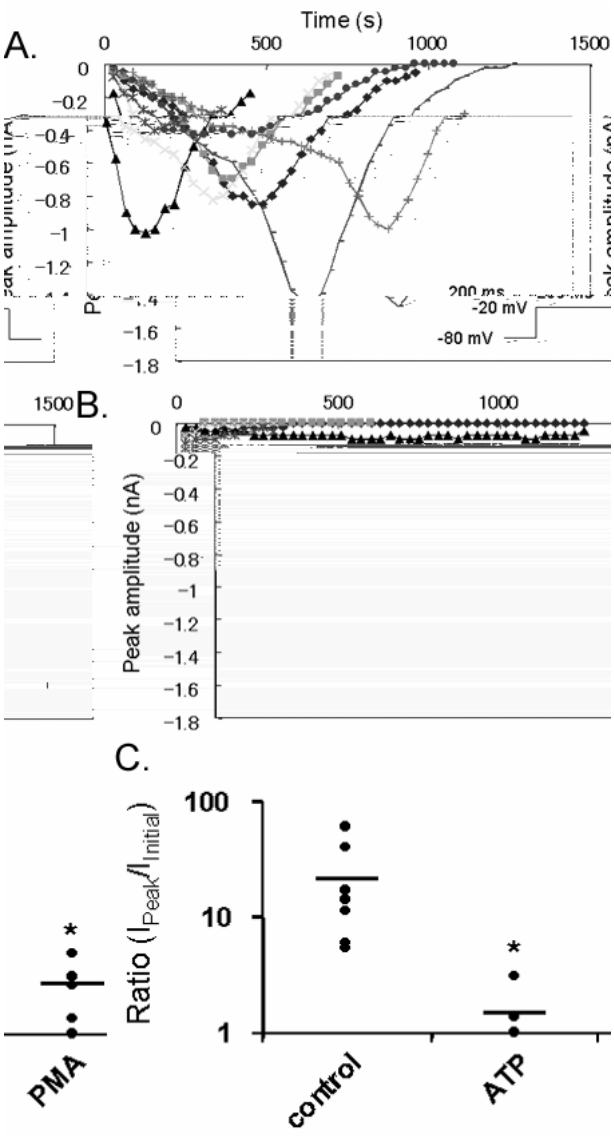
C PKC perforated

Na

$Na_V1.8$ cAMP

20)

PGE_2 TTX Na



7 $Na_V1.9$ ATP PKC

PMA A B 3 mM ATP C

●

*P<0.05

$Na_V1.9$

Na $Na_V1.9$

-60 mV Na

20 mV $Na_V1.9$

ATP PKC PMA

12), 13)

〃 〃

PKC

PKC $Na_V1.9$

3 ATP 3

mM ATP $Na_V1.9$

ATP

ATP

PKC PMA

100 nM PMA

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