

Beta and Muscarinic Receptors in the Human Body

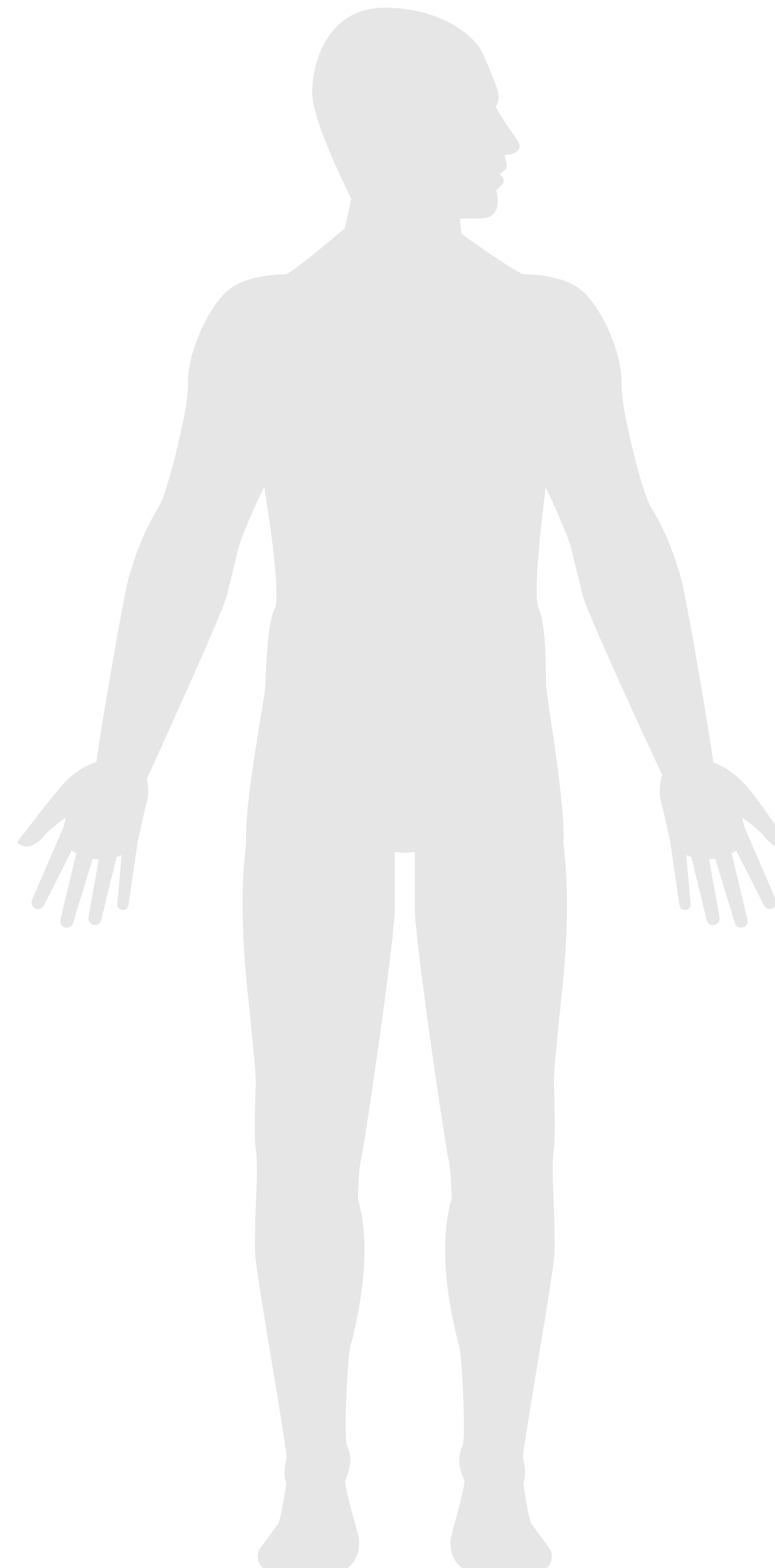
Beta receptor locations throughout the body

β_1

- Cortex
- Cerebellar nuclei
- Brain stem
- Olfactory muscles
- Spinal cord
- Heart
- Kidney
- Adipocytes
- Skeletal muscle

β_3

- Heart
- Adipose tissue
- GI tract
- Smooth muscle (bladder)



β_2

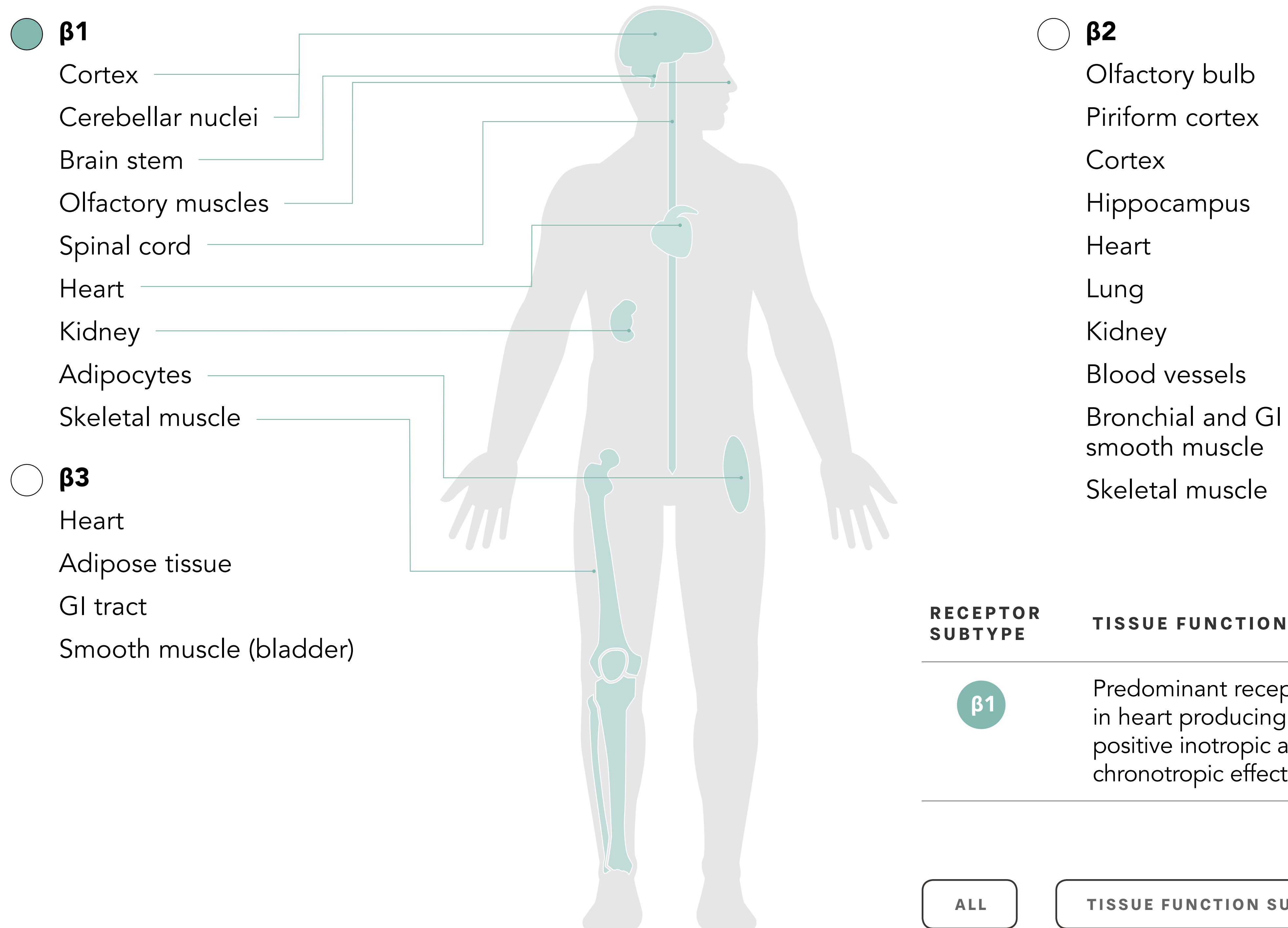
- Olfactory bulb
- Piriform cortex
- Cortex
- Hippocampus
- Heart
- Lung
- Kidney
- Blood vessels
- Bronchial and GI smooth muscle
- Skeletal muscle

ALL

TISSUE FUNCTION SUMMARY

R

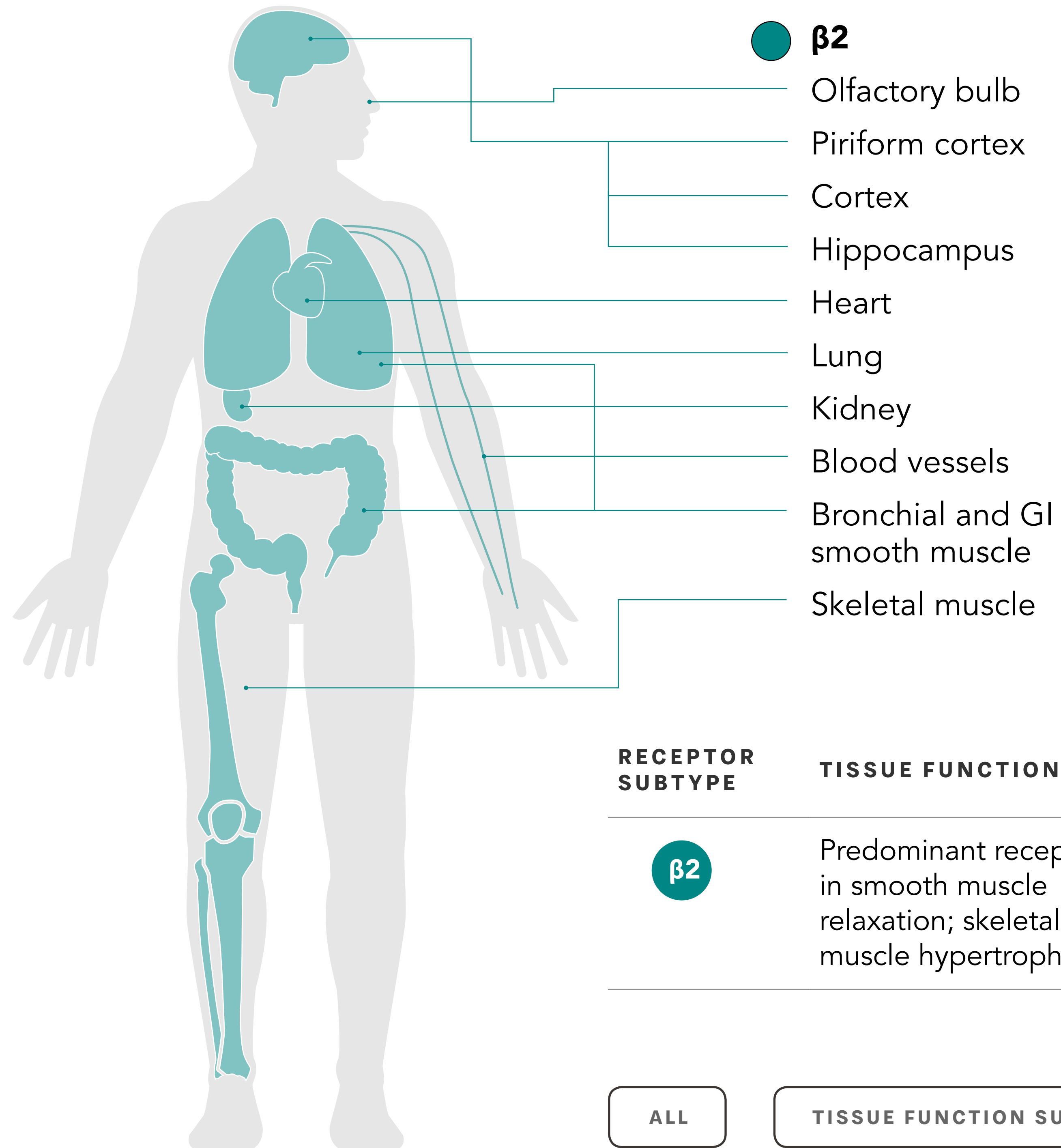
Beta receptor locations throughout the body



Beta receptor locations throughout the body

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 - Cerebellar nuclei
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 - Kidney
 - Adipocytes
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- **β3**
 - Heart
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ALL

TISSUE FUNCTION SUMMARY

Beta receptor locations throughout the body

 β1

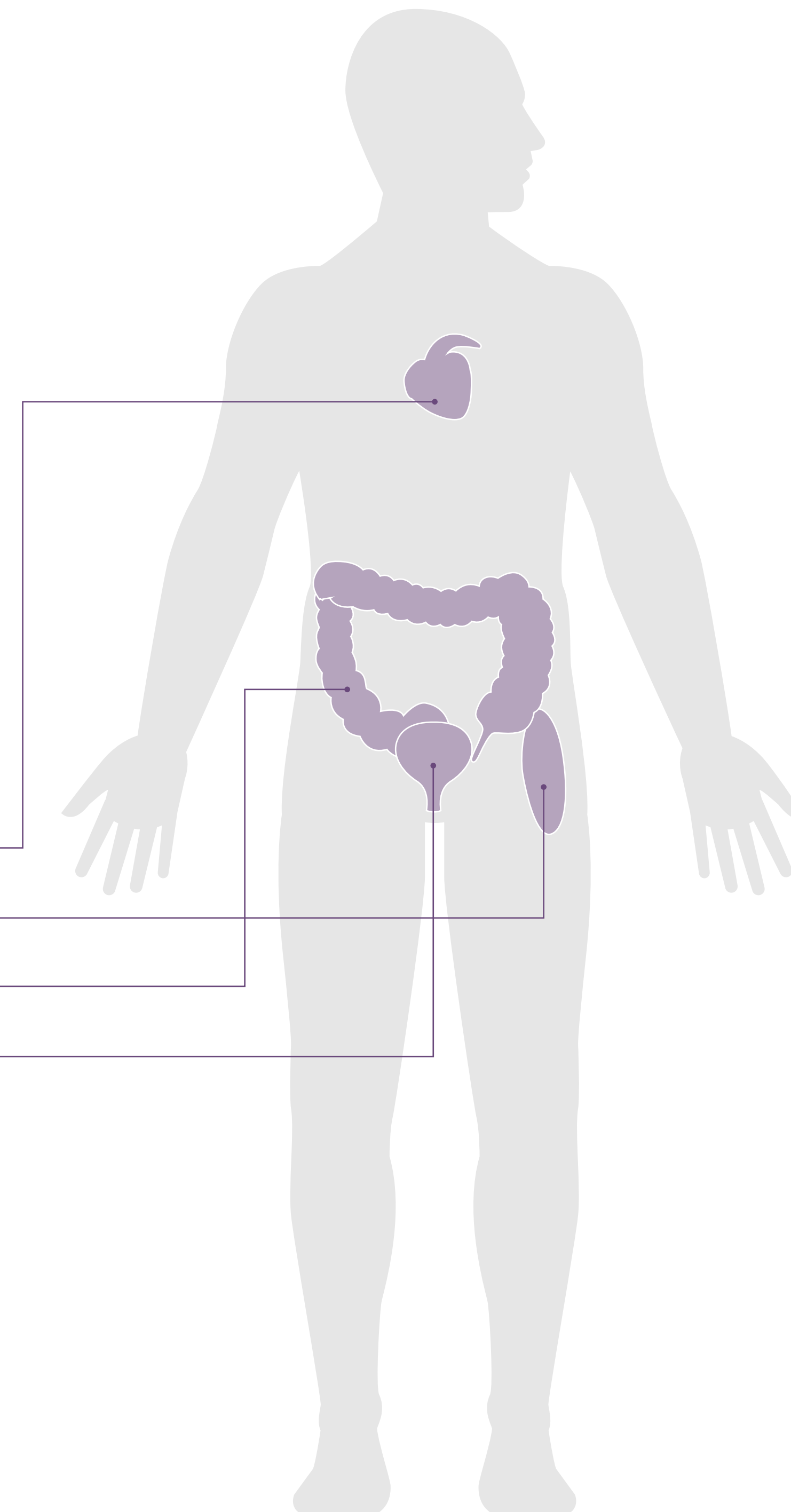
Cortex
Cerebellar nuclei
Brain stem
Olfactory muscles
Spinal cord
Heart
Kidney
Adipocytes
Skeletal muscle

 β3

Heart
Adipose tissue
GI tract
Smooth muscle (bladder)

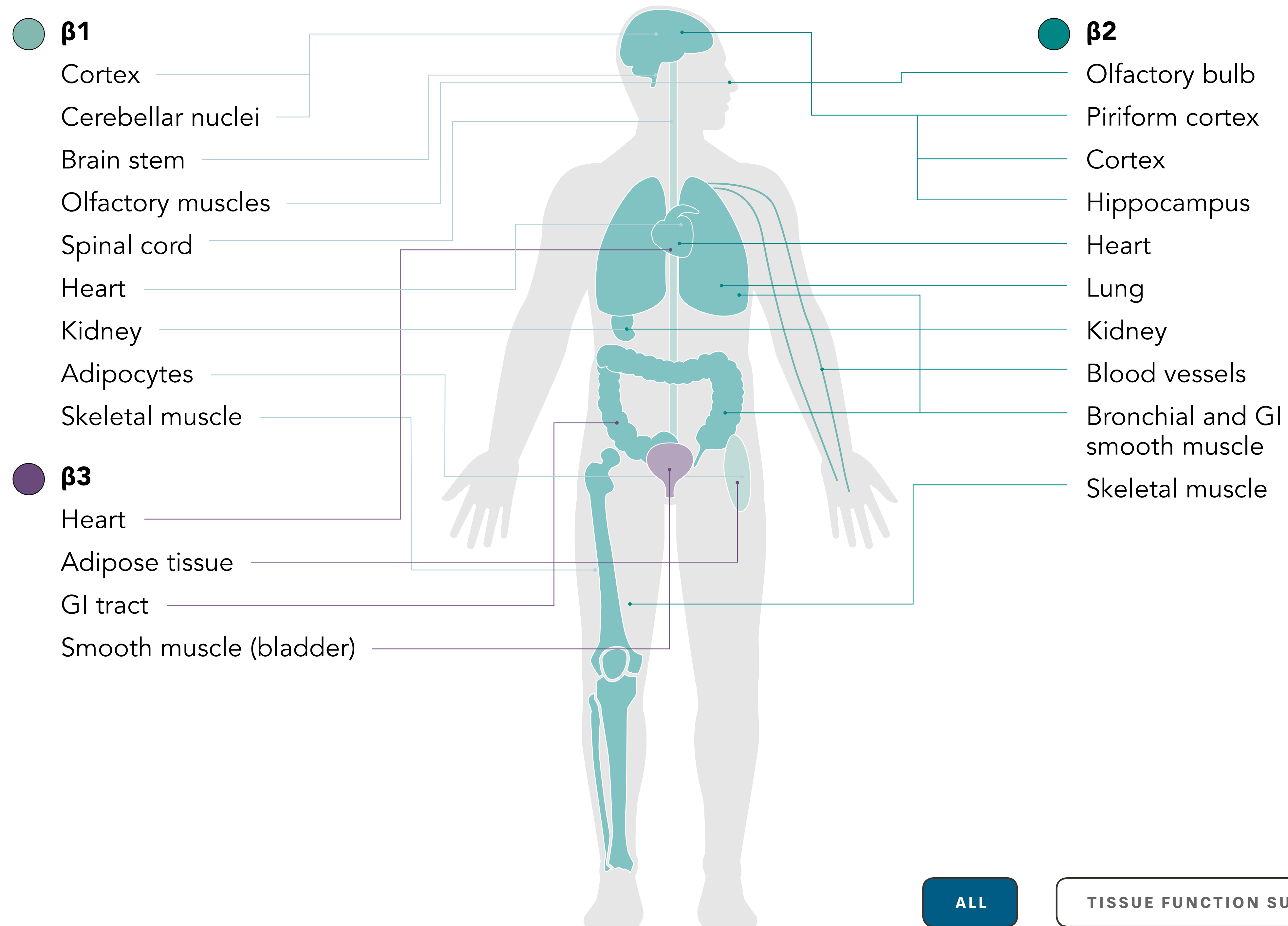
 β2

Olfactory bulb
Piriform cortex
Cortex
Hippocampus
Heart
Lung
Kidney
Blood vessels
Bronchial and GI smooth muscle
Skeletal muscle


RECEPTOR SUBTYPE
TISSUE FUNCTION
 β3

Predominant receptor producing metabolic effects; bladder detrusor muscle relaxation.

Beta receptor locations throughout the body



ALL

TISSUE FUNCTION SUMMARY

R

Beta receptor locations throughout the body

| | RECEPTOR SUBTYPE | TISSUE FUNCTION | |
|---|------------------|---|---|
| <input type="radio"/> β1 Cortex Cerebellar nuclei Brain stem Olfactory mucosa Spinal cord Heart Kidney Adipocytes Skeletal muscle | β1 | Predominant receptor in heart producing positive inotropic and chronotropic effects. | <input type="radio"/> β2 Olfactory bulb Pinniform cortex Cortex Hippocampus Heart Lung Kidney Blood vessels Bronchial and GI smooth muscle Skeletal muscle |
| <input type="radio"/> β3 Heart Adipose tissue GI tract Smooth muscle (bladder) | β3 | Predominant receptor producing metabolic effects; bladder detrusor muscle relaxation. | |

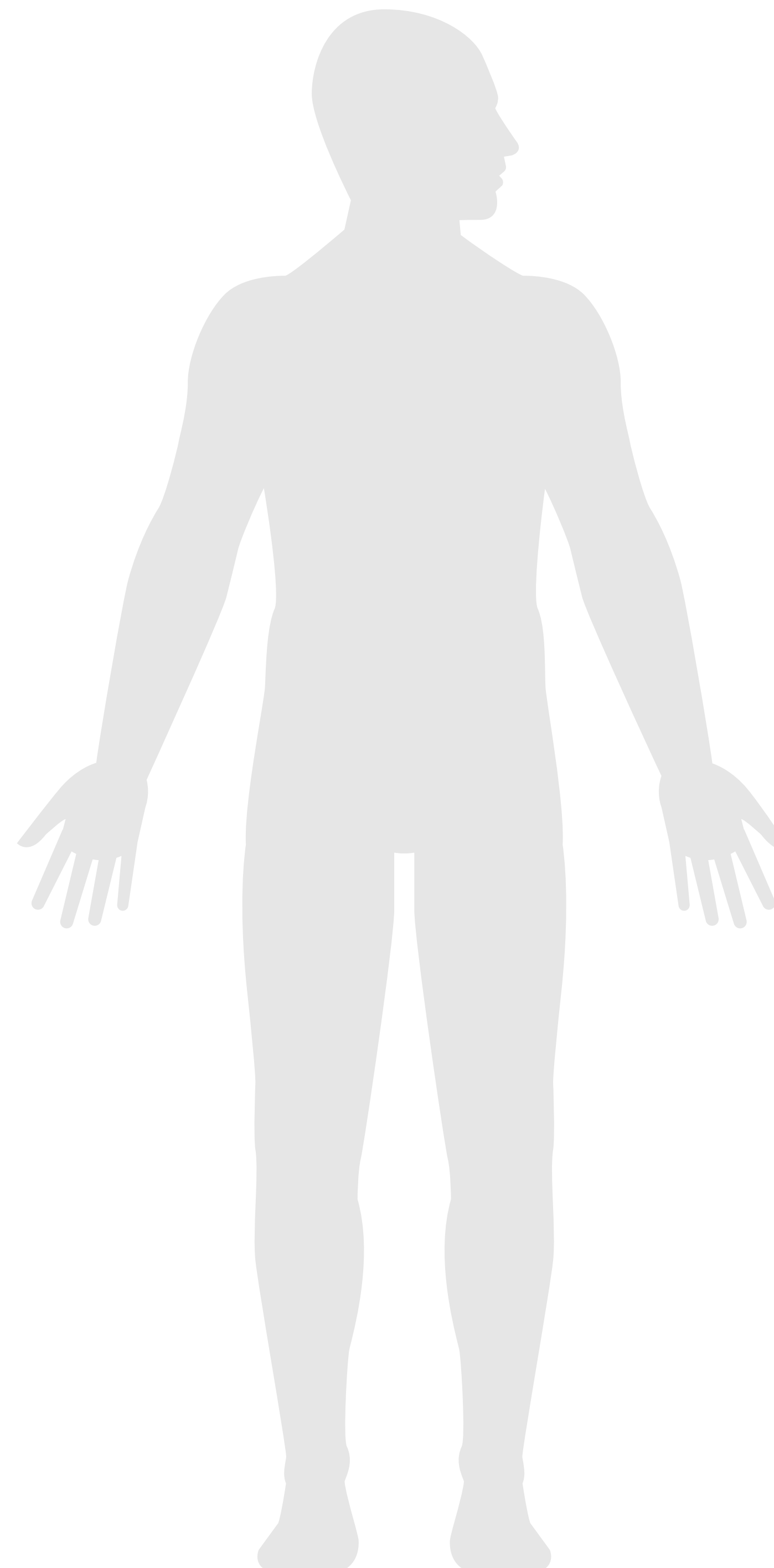
Beta receptor locations throughout the body

 β_1

- Cortex
- Cerebellar nuclei
- Brain stem
- Olfactory muscles
- Spinal cord
- Heart
- Kidney
- Adipocytes
- Skeletal muscle

 β_3

- Heart
- Adipose tissue
- GI tract
- Smooth muscle (bladder)

 **β_2**

- Olfactory bulb
- Piriform cortex
- Cortex
- Hippocampus
- Heart
- Lung
- Kidney
- Blood vessels
- Bronchial and GI smooth muscle
- Skeletal muscle

REFERENCES

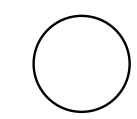
1. Brunton L. et al. *The Pharmacological Basis of Therapeutics, 12th edition*. The McGraw-Hill Companies, Inc., 2011. Print.
2. Igawa Y. et al. *Br J Pharmacol*. 1999;126:819-825.

ALL

TISSUE FUNCTION SUMMARY

R

Muscarinic receptor locations throughout the body

**M₁**

CNS

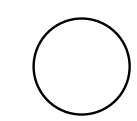
(most abundant in cerebral cortex, hippocampus, striatum and thalamus)

Autonomic ganglia

Gastric glands

Salivary glands

Enteric nerves

**M₂**

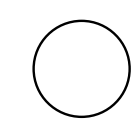
CNS

(hind brain, thalamus, cerebral cortex, hippocampus, striatum)

Heart

Smooth muscle

Autonomic nerve terminals

**M₃**

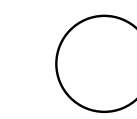
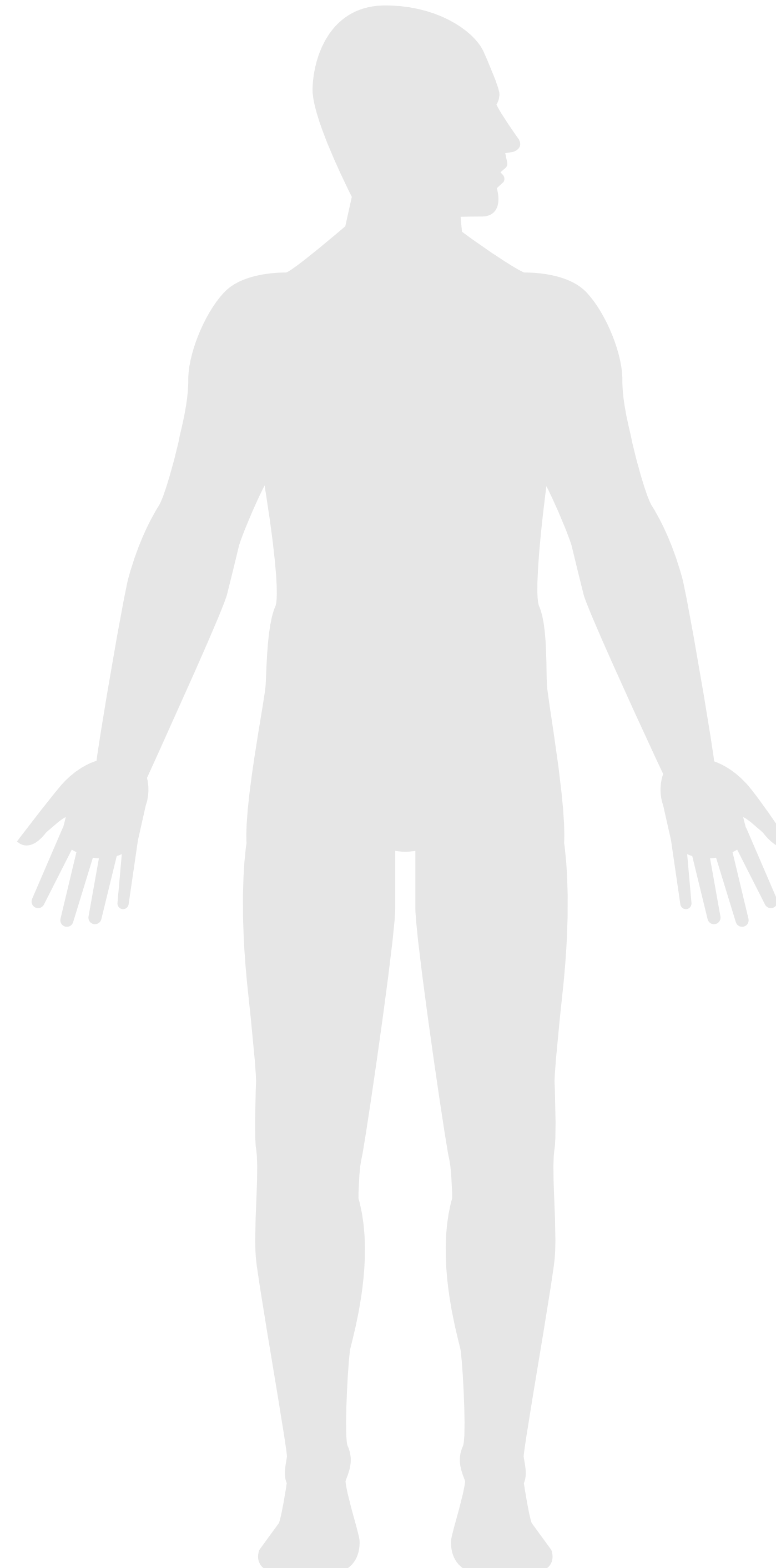
CNS

(cerebral cortex, hippocampus)

Smooth muscle

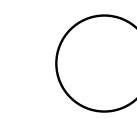
Salivary glands

Heart

**M₄**

CNS

(particularly forebrain, striatum, cerebral cortex, hippocampus)

**M₅**

Substantia nigra

(predominant in mAChR in neurons in VTA and substantia nigra)

CNS

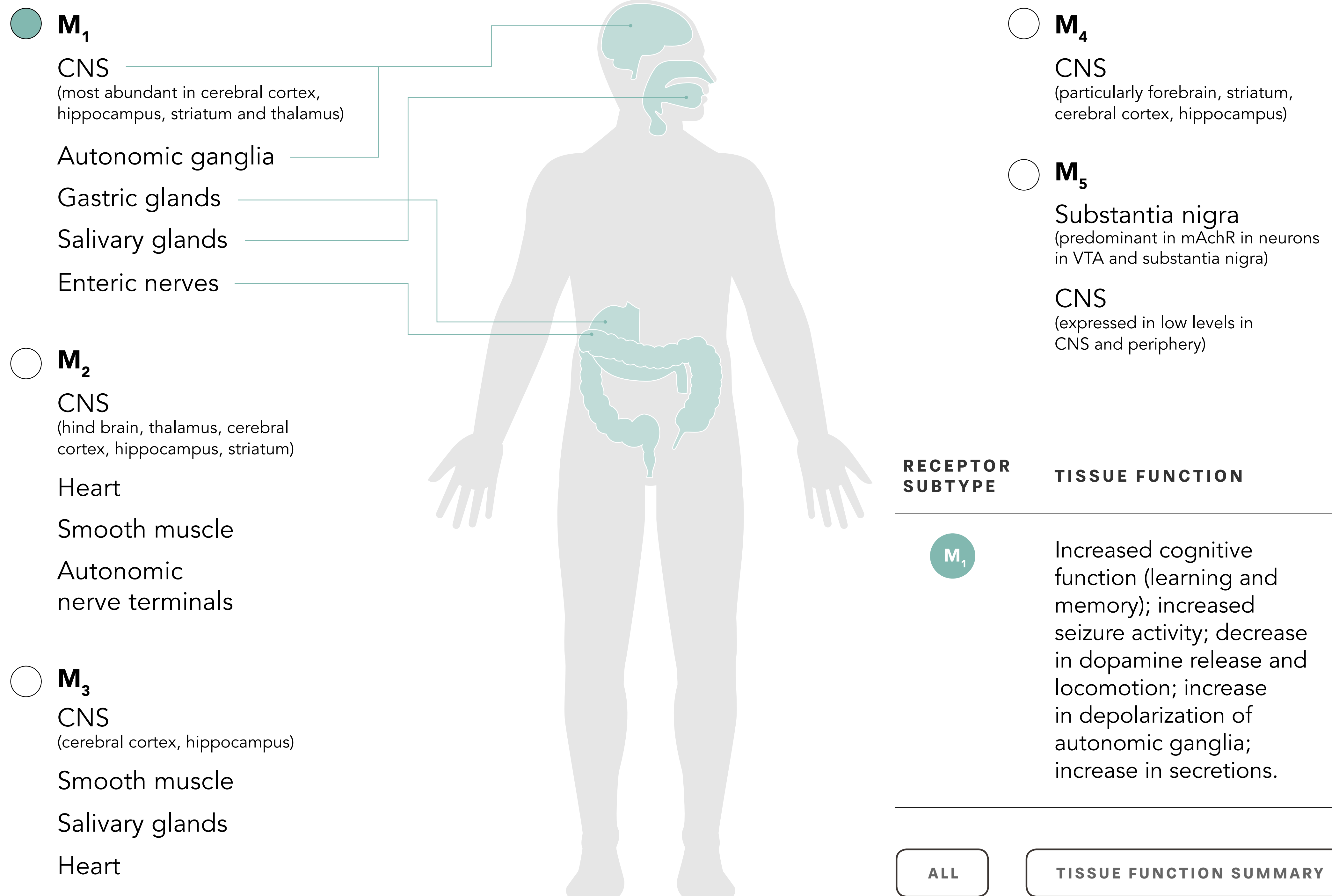
(expressed in low levels in CNS and periphery)

ALL

TISSUE FUNCTION SUMMARY

R

Muscarinic receptor locations throughout the body



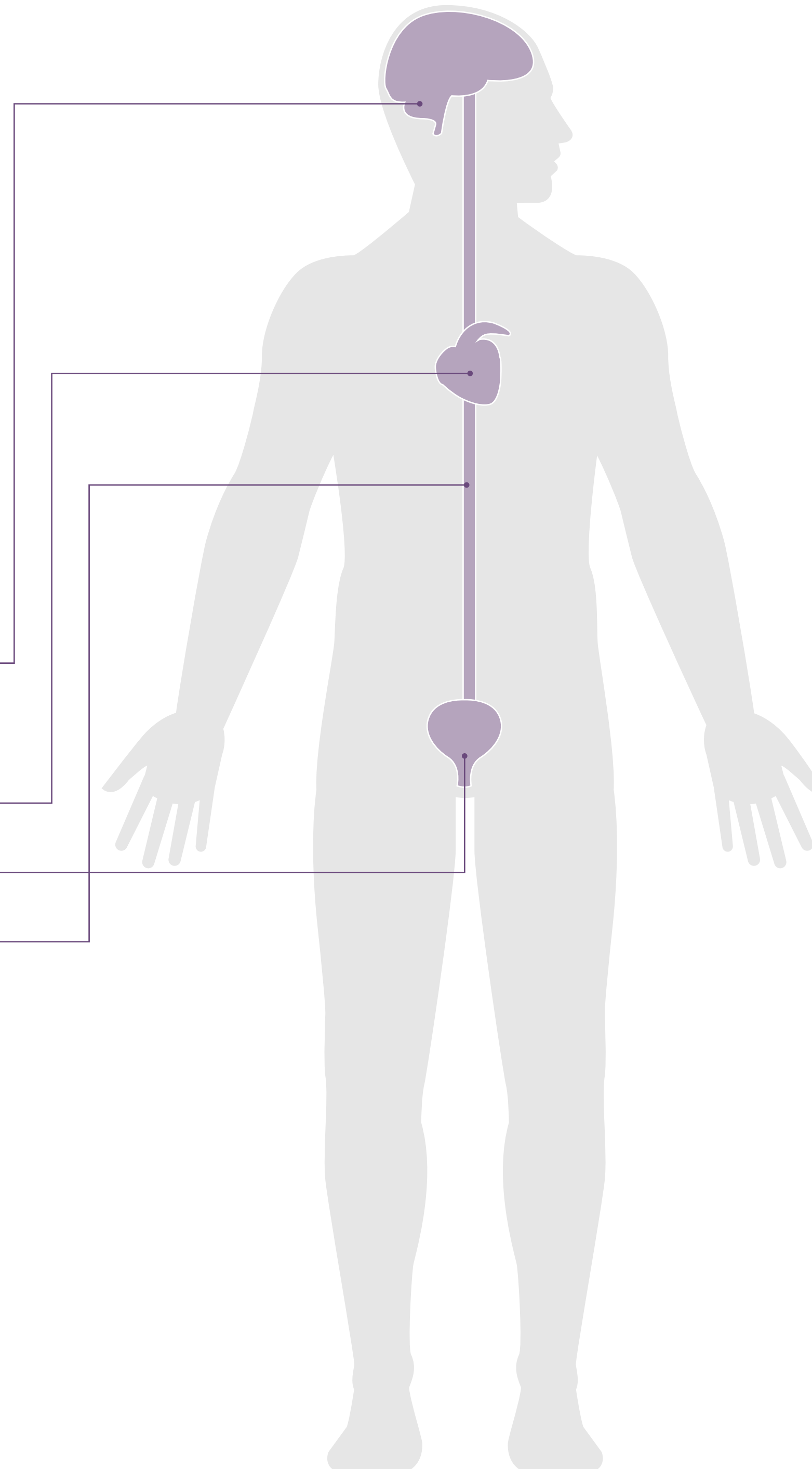
ALL

TISSUE FUNCTION SUMMARY

R

Muscarinic receptor locations throughout the body

- M₁**
CNS
(most abundant in cerebral cortex, hippocampus, striatum and thalamus)
Autonomic ganglia
Gastric glands
Salivary glands
Enteric nerves
- M₂**
CNS
(hind brain, thalamus, cerebral cortex, hippocampus, striatum)
Heart
Smooth muscle
Autonomic nerve terminals
- M₃**
CNS
(cerebral cortex, hippocampus)
Smooth muscle
Salivary glands
Heart



- M₄**
CNS
(particularly forebrain, striatum, cerebral cortex, hippocampus)
- M₅**
Substantia nigra
(predominant in mAChR in neurons in VTA and substantia nigra)
CNS
(expressed in low levels in CNS and periphery)

RECEPTOR SUBTYPE

TISSUE FUNCTION

M₂

In the heart, impacts the SA node (slowed spontaneous depolarization, hyperpolarization, decreased heart rate), AV node (decrease in conduction velocity), atrium (reduced refractory period, reduced contraction) and ventricle (slight decrease in contraction). Increased contraction of smooth muscle. In peripheral nerves causes neural inhibition via autoreceptors and heteroreceptors, as well as decreased ganglionic transmission. In the CNS causes neural inhibition, increased tremors, hypothermia, and analgesia.

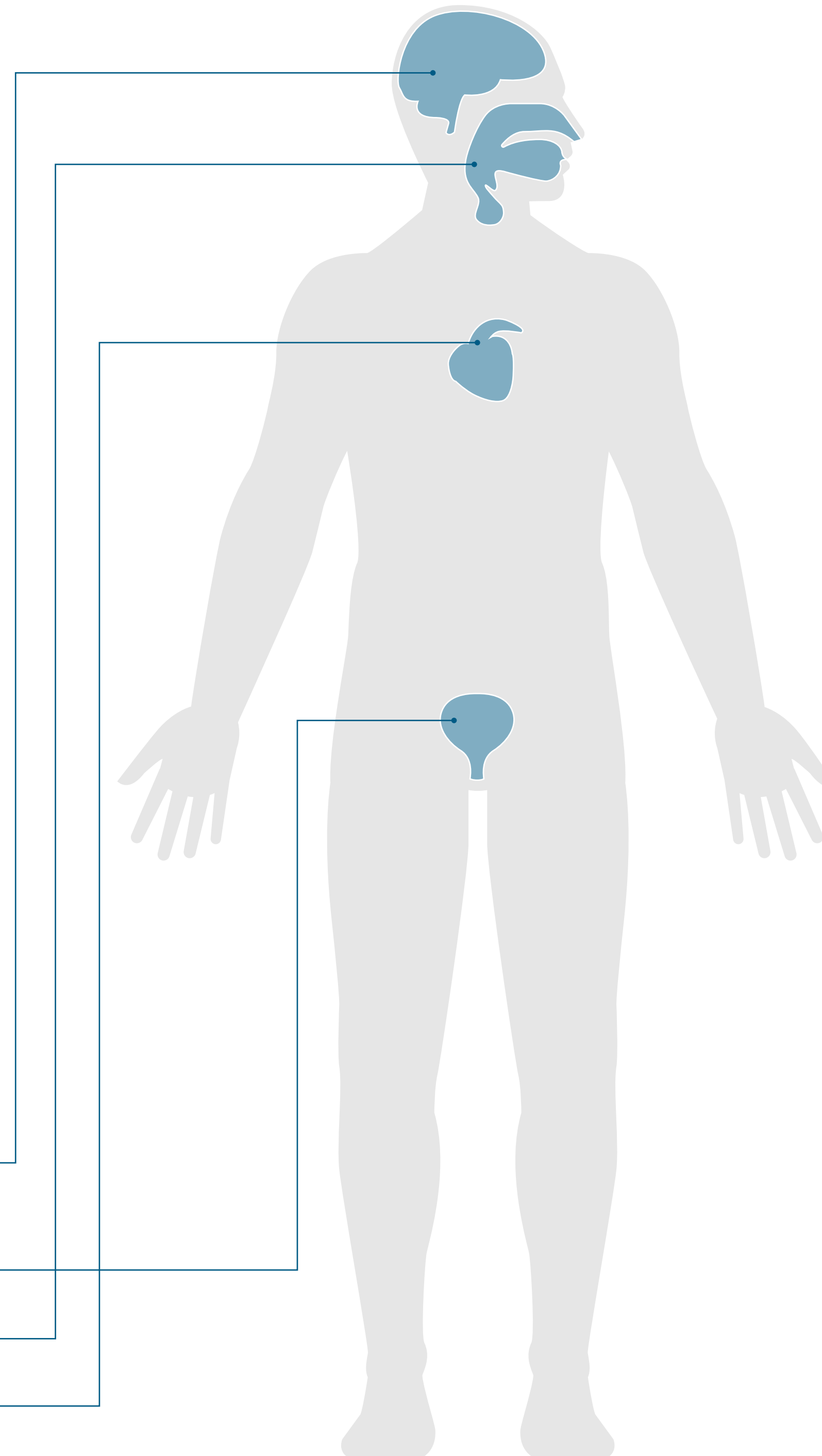
ALL

TISSUE FUNCTION SUMMARY

R

Muscarinic receptor locations throughout the body

- M₁**
CNS
(most abundant in cerebral cortex, hippocampus, striatum and thalamus)
Autonomic ganglia
Gastric glands
Salivary glands
Enteric nerves
- M₂**
CNS
(hind brain, thalamus, cerebral cortex, hippocampus, striatum)
Heart
Smooth muscle
Autonomic nerve terminals
- M₃**
CNS
(cerebral cortex, hippocampus)
Smooth muscle
Salivary glands
Heart



- M₄**
CNS
(particularly forebrain, striatum, cerebral cortex, hippocampus)
- M₅**
Substantia nigra
(predominant in mAChR in neurons in VTA and substantia nigra)
CNS
(expressed in low levels in CNS and periphery)

RECEPTOR
SUBTYPE

TISSUE FUNCTION

M₃

Increased smooth muscle contraction (eg. bladder detrusor muscle); increased secretion (predominantly in salivary gland); increased food intake, body weight fat deposits; inhibition of dopamine release; synthesis of nitric oxide.

ALL

TISSUE FUNCTION SUMMARY

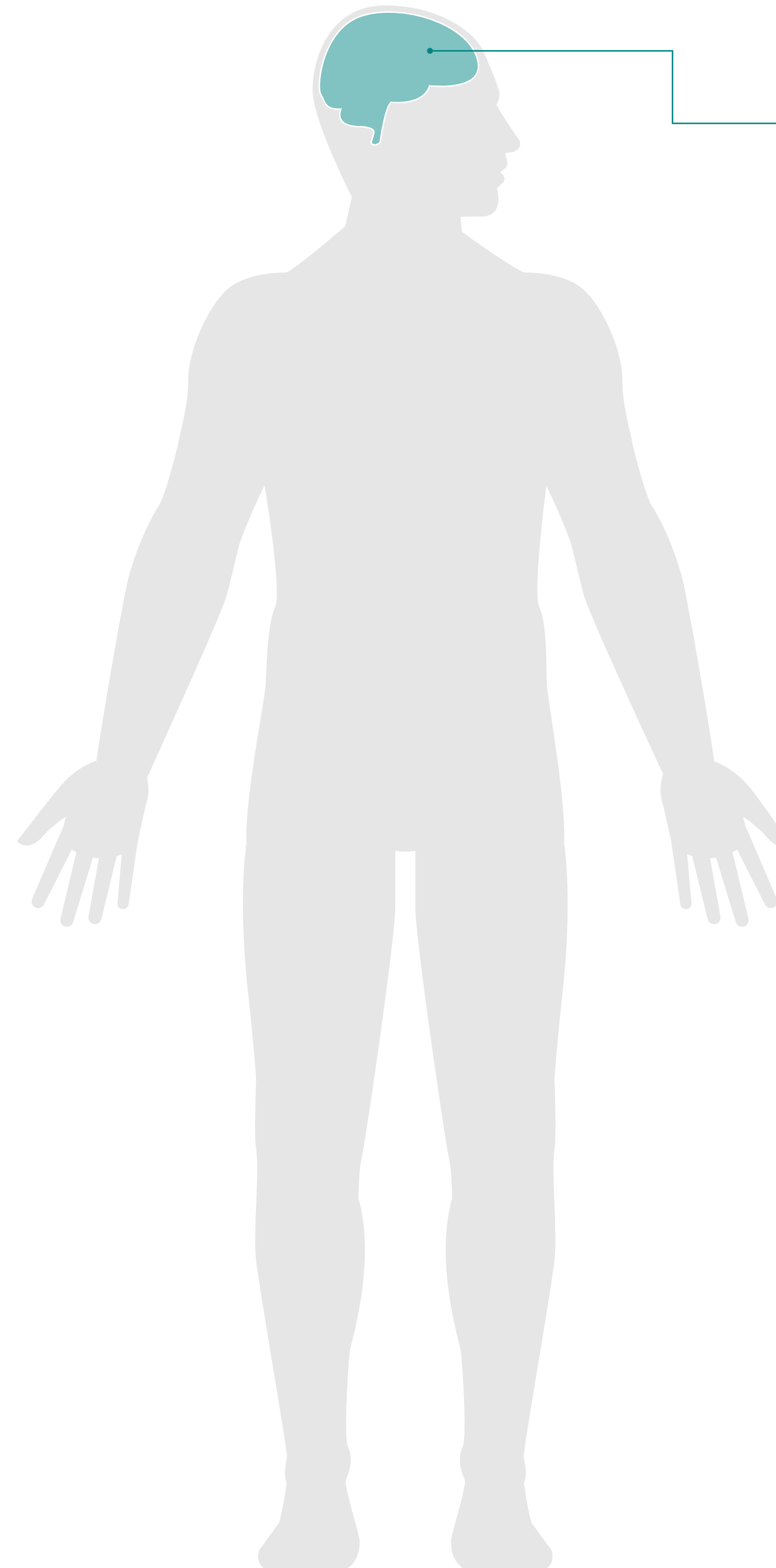
R

Muscarinic receptor locations throughout the body

- M₁**
 CNS
 (most abundant in cerebral cortex, hippocampus, striatum and thalamus)
- Autonomic ganglia
 Gastric glands
 Salivary glands
 Enteric nerves

- M₂**
 CNS
 (hind brain, thalamus, cerebral cortex, hippocampus, striatum)
- Heart
 Smooth muscle
 Autonomic nerve terminals

- M₃**
 CNS
 (cerebral cortex, hippocampus)
- Smooth muscle
 Salivary glands
 Heart



- M₄**
 CNS
 (particularly forebrain, striatum, cerebral cortex, hippocampus)

- M₅**
 Substantia nigra
 (predominant in mAChR in neurons in VTA and substantia nigra)
- CNS
 (expressed in low levels in CNS and periphery)

RECEPTOR
SUBTYPE

TISSUE FUNCTION

M₄

Autoreceptor- and heteroreceptor-mediated inhibition of transmitter release in CNS and periphery; analgesia; cataleptic activity; facilitation of dopamine release.

ALL

TISSUE FUNCTION SUMMARY

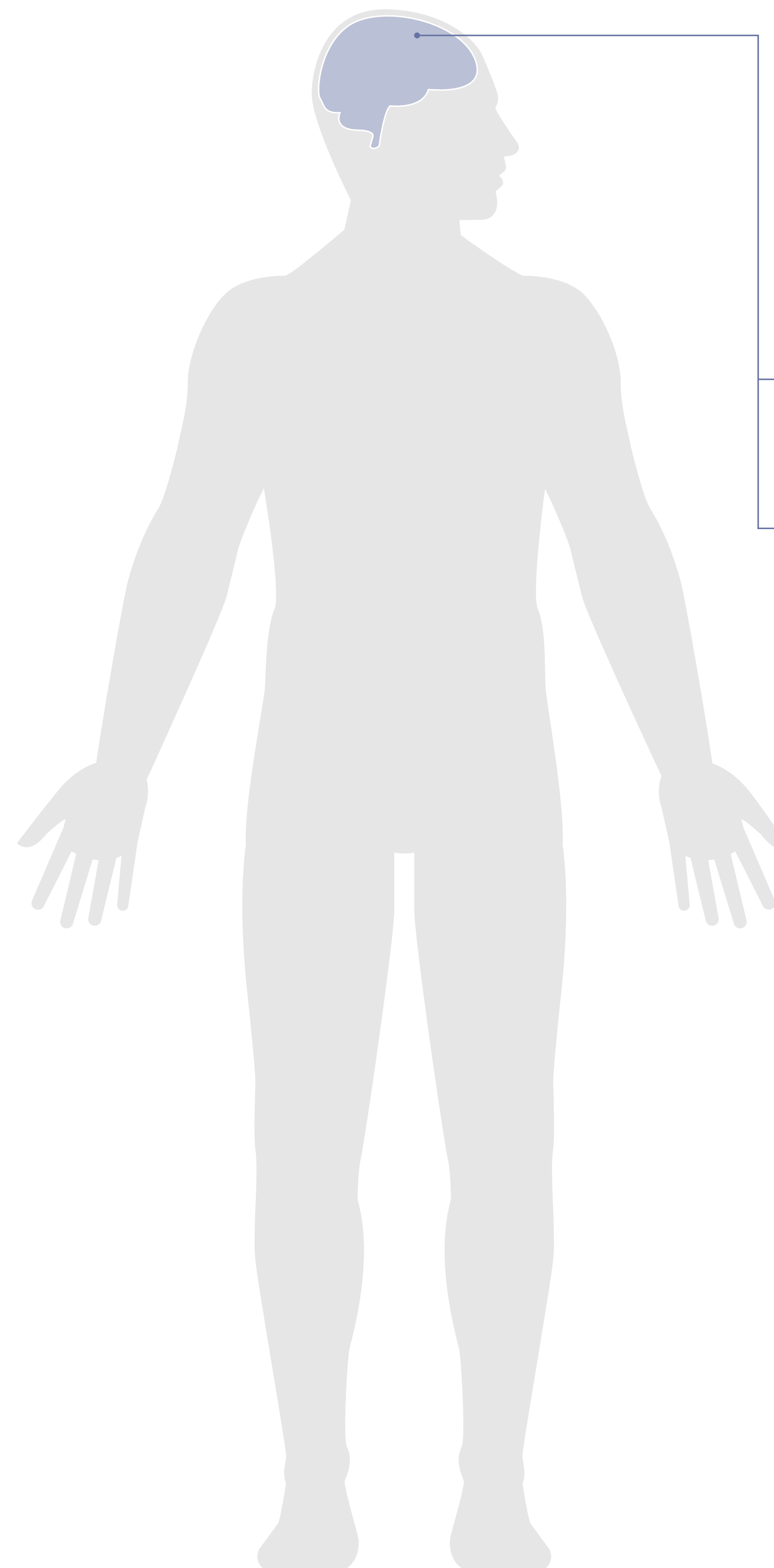
(R)

Muscarinic receptor locations throughout the body

- **M₁**
CNS
(most abundant in cerebral cortex, hippocampus, striatum and thalamus)
Autonomic ganglia
Gastric glands
Salivary glands
Enteric nerves

- **M₂**
CNS
(hind brain, thalamus, cerebral cortex, hippocampus, striatum)
Heart
Smooth muscle
Autonomic nerve terminals

- **M₃**
CNS
(cerebral cortex, hippocampus)
Smooth muscle
Salivary glands
Heart



- **M₄**
CNS
(particularly forebrain, striatum, cerebral cortex, hippocampus)
- **M₅**
Substantia nigra
(predominant in mAChR in neurons in VTA and substantia nigra)
CNS
(expressed in low levels in CNS and periphery)

RECEPTOR
SUBTYPE

TISSUE FUNCTION

M₅

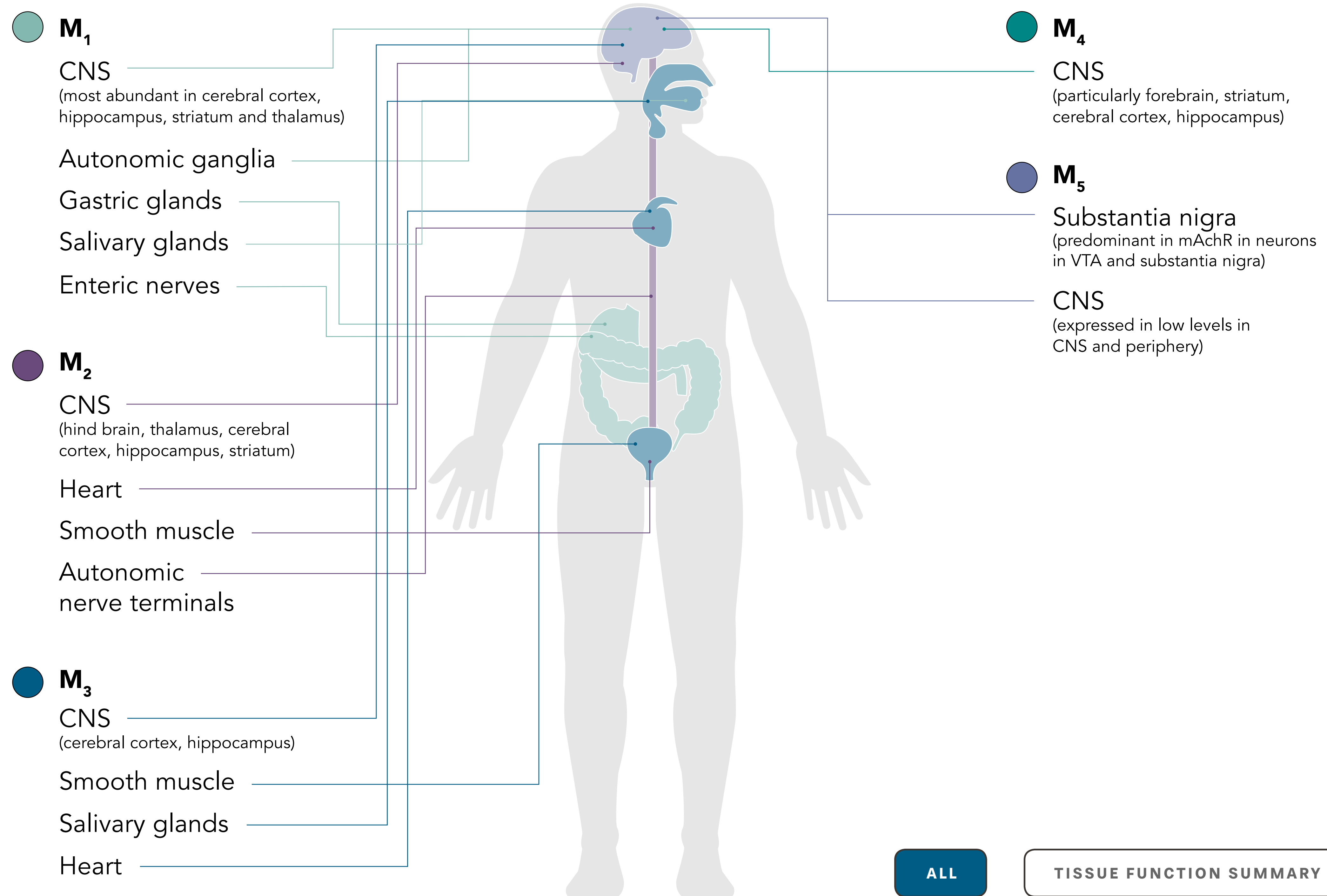
Mediator of dilation in cerebral arteries and arterioles; facilitates dopamine release; augmentation of drug-seeking behaviour and reward.

ALL

TISSUE FUNCTION SUMMARY

R

Muscarinic receptor locations throughout the body



ALL

TISSUE FUNCTION SUMMARY

R

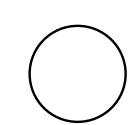
RECEPTOR
SUBTYPE

TISSUE FUNCTION



| RECEPTOR SUBTYPE | TISSUE FUNCTION |
|--|---|
| <input checked="" type="radio"/> M₁ <input type="radio"/> M ₁ CNS (most abundant in cerebral cortex, hippocampus, striatum and thalamus) | Increased cognitive function (learning and memory); increased seizure activity; decrease in dopamine release and locomotion; increase in depolarization of autonomic ganglia; increase in secretions. |
| <input type="radio"/> M₂ <input type="radio"/> M ₂ Autonomic ganglia Gastric glands Salivary glands Enteric nerves CNS (hindbrain, thalamus, cerebral cortex, hippocampus, striatum) | In the heart, impacts the SA node (slowed spontaneous depolarization, hyperpolarization, decreased heart rate), AV node (decrease in conduction velocity), atrium (reduced refractory period, reduced contraction) and ventricle (slight decrease in contraction). Increased contraction of smooth muscle. In peripheral nerves causes neural inhibition via autoreceptors and heteroreceptors, as well as decreased ganglionic transmission. In the CNS causes neural inhibition, increased tremors, hypothermia, and analgesia. |
| <input type="radio"/> M₃ <input type="radio"/> M ₃ Heart Smooth muscle Autonomic nerve terminals | Increased smooth muscle contraction (eg. bladder detrusor muscle); increased secretion (predominantly in salivary gland); increased food intake, body weight fat deposits; inhibition of dopamine release; synthesis of nitric oxide. |
| <input type="radio"/> M₄ <input type="radio"/> M ₄ CNS (expressed in low levels in CNS and periphery) | Autoreceptor- and heteroreceptor-mediated inhibition of transmitter release in CNS and periphery; analgesia; cataleptic activity; facilitation of dopamine release. |
| <input type="radio"/> M₅ <input type="radio"/> M ₅ CNS (cerebral cortex, hippocampus) Smooth muscle Salivary glands Heart | Mediator of dilation in cerebral arteries and arterioles; facilitates dopamine release; augmentation of drug-seeking behaviour and reward. |

Muscarinic receptor locations throughout the body

**M₁**

CNS

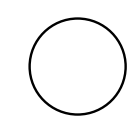
(most abundant in cerebral cortex, hippocampus, striatum and thalamus)

Autonomic ganglia

Gastric glands

Salivary glands

Enteric nerves

**M₂**

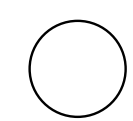
CNS

(hind brain, thalamus, cerebral cortex, hippocampus, striatum)

Heart

Smooth muscle

Autonomic nerve terminals

**M₃**

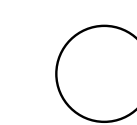
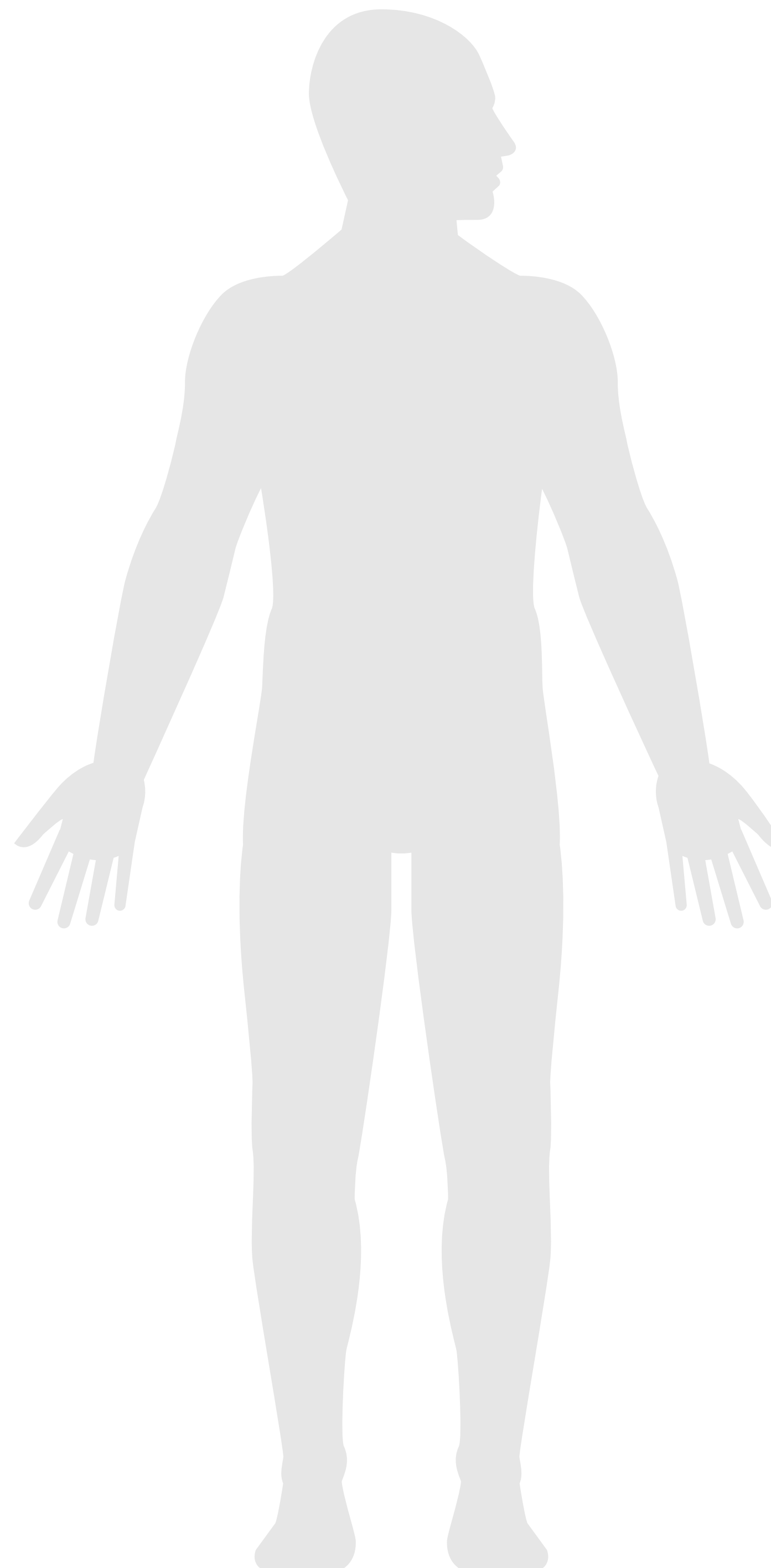
CNS

(cerebral cortex, hippocampus)

Smooth muscle

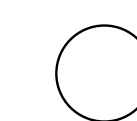
Salivary glands

Heart

**M₄**

CNS

(particularly forebrain, striatum, cerebral cortex, hippocampus)

**M₅**

Substantia nigra

(predominant in mAChR in neurons in VTA and substantia nigra)

CNS

(expressed in low levels in CNS and periphery)

REFERENCE

1. Brunton L. *et al. The Pharmacological Basis of Therapeutics, 12th edition.* The McGraw-Hill Companies, Inc., 2011. Print.

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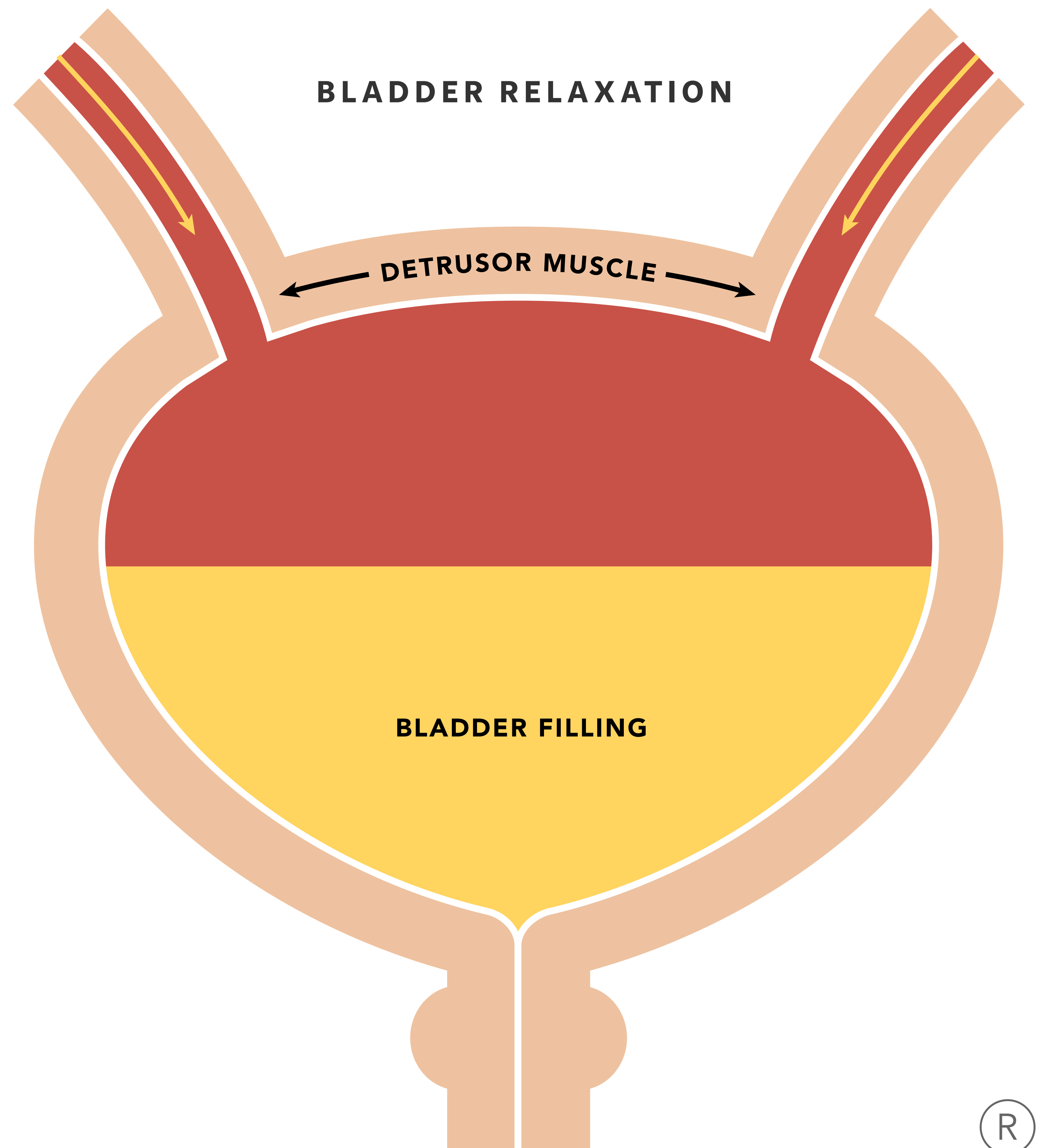
TISSUE FUNCTION SUMMARY

R

Role of beta receptors in the bladder

Beta adrenoceptors help mediate detrusor muscle relaxation¹⁻³

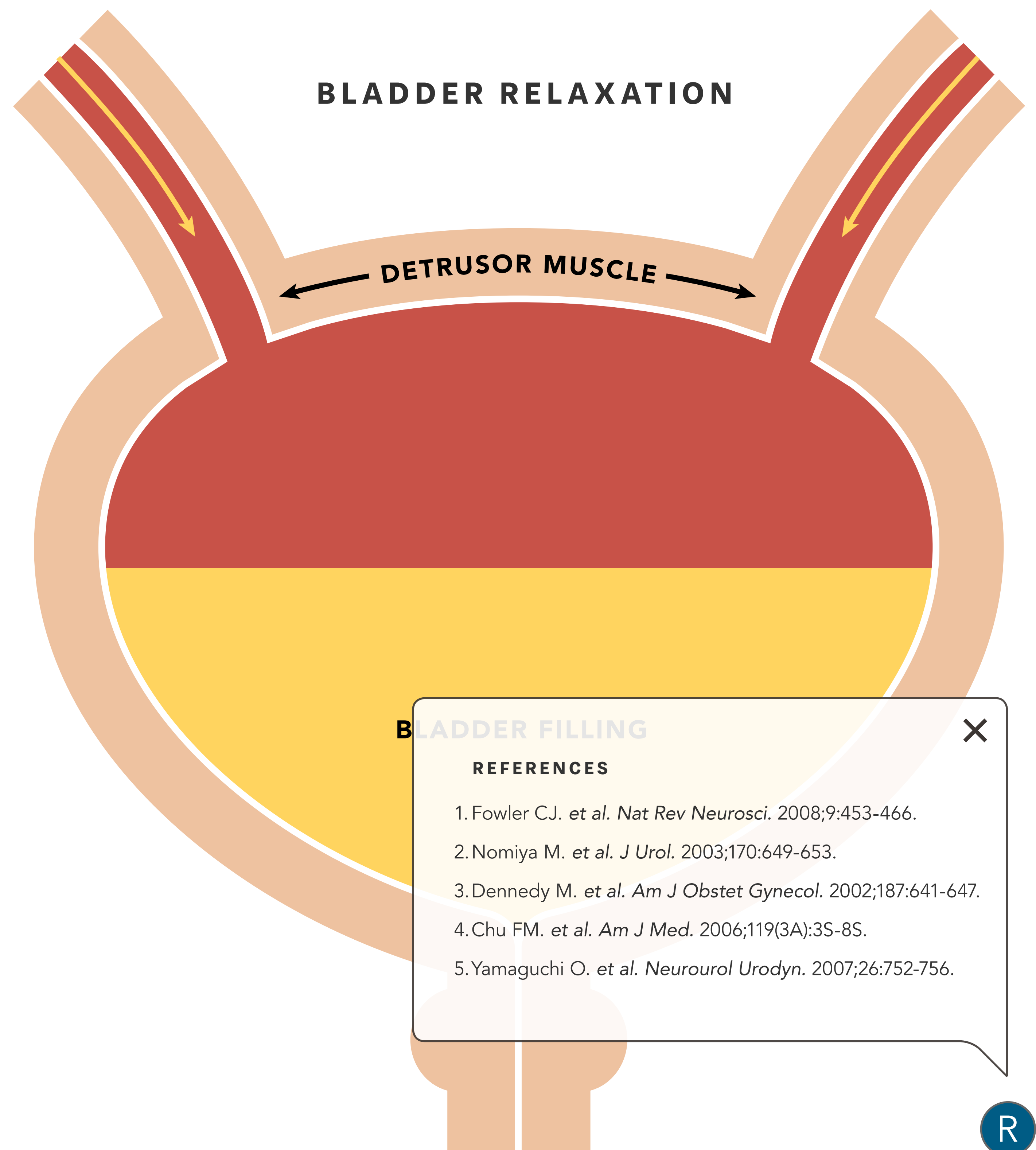
- Beta receptors are part of the sympathetic autonomic nervous system (ANS), which controls the micturition cycle¹
- Storage, which makes up the majority of the micturition cycle, is predominantly regulated by the sympathetic ANS via the neurotransmitter norepinephrine^{1,4}
- Beta adrenoceptors are highly concentrated in the detrusor muscle in the bladder. Here, norepinephrine activates beta receptors causing detrusor muscle relaxation¹⁻³
- Beta receptor activation increases bladder filling capacity without impacting the voiding process⁵



Role of beta receptors in the bladder

Beta adrenoceptors help mediate detrusor muscle relaxation¹⁻³

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BLADDER FILLING

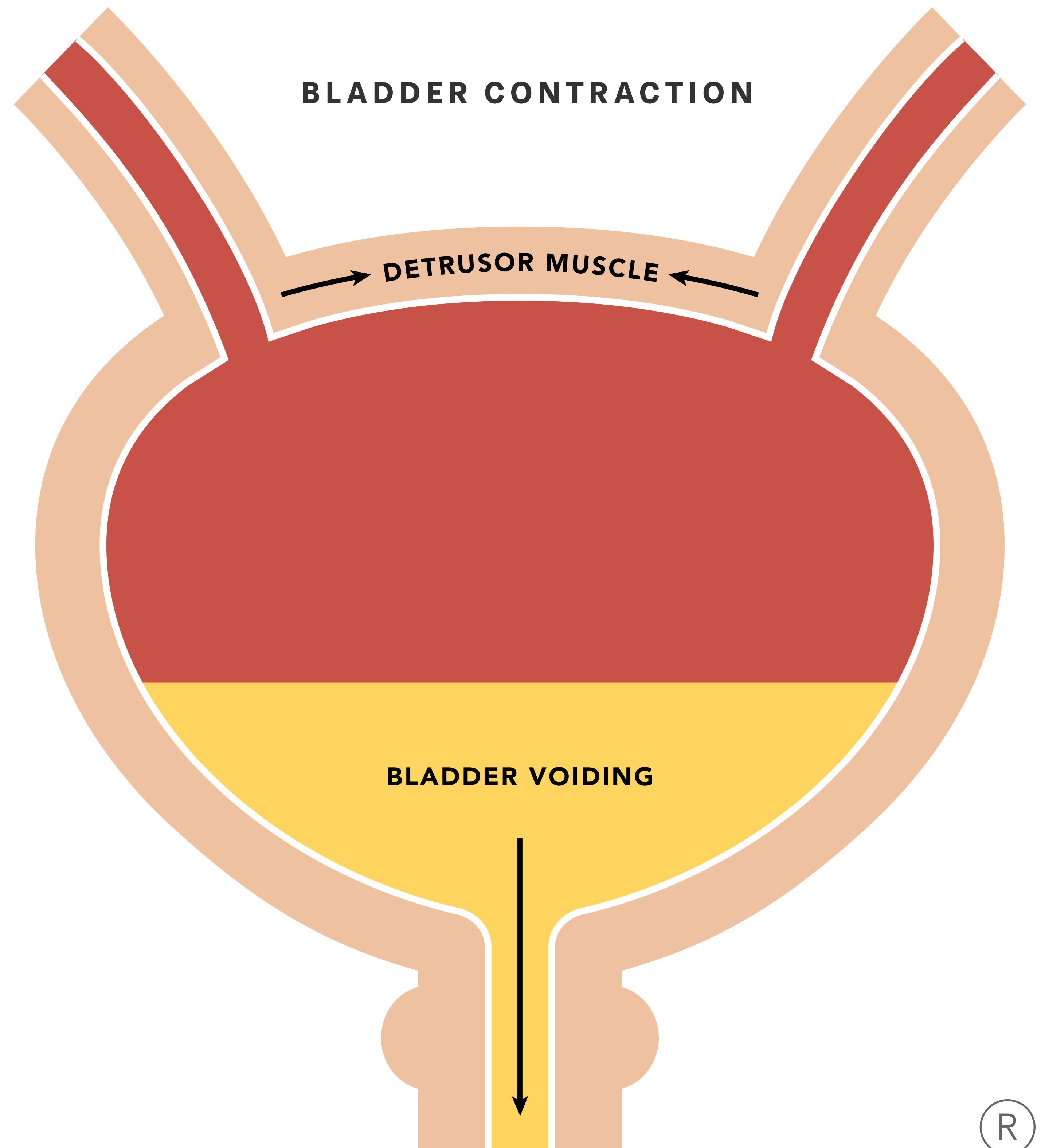
REFERENCES

1. Fowler CJ. et al. *Nat Rev Neurosci.* 2008;9:453-466.
2. Nomiya M. et al. *J Urol.* 2003;170:649-653.
3. Denny M. et al. *Am J Obstet Gynecol.* 2002;187:641-647.
4. Chu FM. et al. *Am J Med.* 2006;119(3A):3S-8S.
5. Yamaguchi O. et al. *Neurourol Urodyn.* 2007;26:752-756.

Role of muscarinic receptors in the bladder

Antimuscarinics help prohibit detrusor muscle contraction^{1,2}

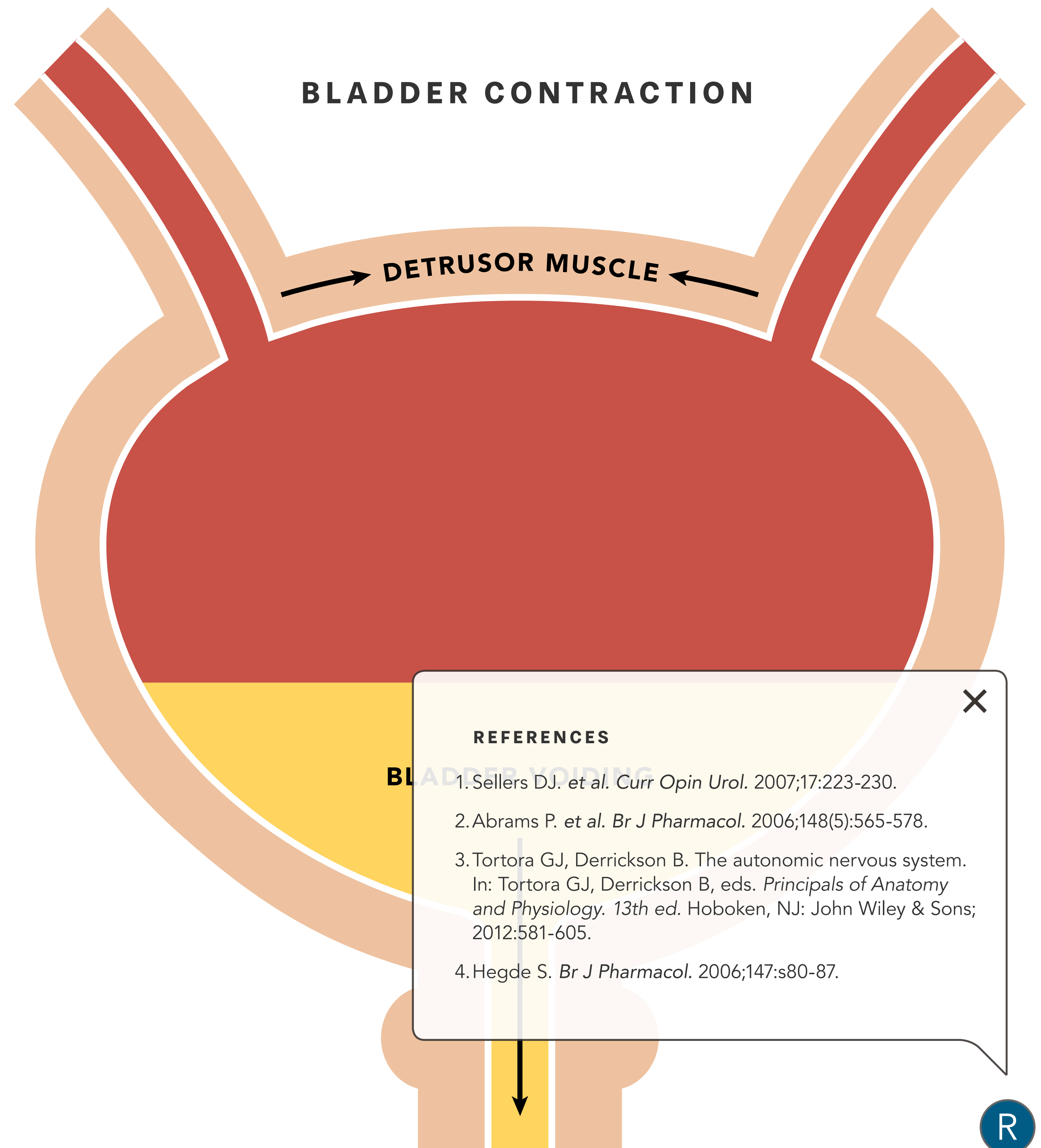
- Muscarinic (cholinergic) receptors bind to acetylcholine as part of the parasympathetic autonomic nervous system (ANS) to help regulate the urinary tract³
- Antimuscarinics, a subclass of anticholinergics, act on muscarinic receptors throughout the body to mediate distinct physiological functions based on location and receptor type selectivity²
- Acetylcholine binds to muscarinic receptors in the detrusor muscle to elicit bladder contraction^{2,4}
- Antimuscarinics inhibit M_2 and M_3 receptors in order to limit detrusor muscle contraction and help control bladder voiding¹



Role of muscarinic receptors in the bladder

Antimuscarinics help prohibit detrusor muscle contraction^{1,2}

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- Antimuscarinics, a subclass of anticholinergics, act on muscarinic receptors throughout the body to mediate distinct physiological functions based on location and receptor type selectivity²
- Acetylcholine binds to muscarinic receptors in the detrusor muscle to elicit bladder contraction^{2,4}
- Antimuscarinics inhibit M₂ and M₃ receptors in order to limit detrusor muscle contraction and help control bladder voiding¹



MOD of beta and muscarinic receptors in the bladder

