Scientists unlock the 'gates' on sudden cardiac death (w/ Video)

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Australian researchers have come one step closer to understanding how the rhythm of the heartbeat is controlled and why many common drugs, including some antibiotics, antihistamines and anti-psychotics, can cause a potentially fatal abnormal heart rhythm.

It is estimated around 40-50% of all drugs in development will block one of the main 'channels' that carries electricity in the heart and, as a result, can cause heart rhythm problems called cardiac arrhythmias. Most sudden cardiac deaths are caused by cardiac arrhythmias.

Since 1996, nine drugs have been withdrawn from the market or had their use severely restricted due to this serious side effect.

In a paper published in this month's edition of the prestigious journal Nature Structural and Molecular Biology, scientists from the Victor Chang Institute in Sydney have discovered a key clue as to why this happens, by understanding how the 'gates,' which effectively 'open' and 'close' the channel, operate.

"Just like a set of metal wires that carry electricity to light up our streets, our body has a series of channels that carry tiny charged particles called ions, into and out of cells, to trigger a heartbeat," said Professor Jamie Vandenberg, Head of the Cardiac Electrophysiology Laboratory at the Victor Chang Institute.

"Depending on the position of these gates, many common drugs bind, or

attach themselves to these channels, blocking the ions from passing through. This causes what we call Long QT syndrome, where the length of the heart beat is longer than usual, which greatly increases the risk of arrhythmia."

The group of drugs most commonly associated with this side effect are anti-psychotic drugs, taken by patients with schizophrenia and other psychiatric disorders. Patients taking these drugs are up to three times more likely to die of sudden cardiac death due to an abnormal heart rhythm.

The team of researchers, led by Professor Vandenberg, studied the hERG potassium channel, an ion channel that determines how long each heart beat lasts and the channel which is most susceptible to being 'blocked' by drugs.

"The hERG channel is a particularly 'sticky' channel, in that most drugs will bind to it when the outer gate is closed. What we've done is to discover how these outer gates operate, in the hope that we can then design drugs more effectively to minimise the unwanted side effects," said Professor Vandenberg.

"The gates to this channel operate in a much more complex way than was previously thought – much like a Japanese puzzle box, they require a series of complicated, interrelated movements to open them. It is not simply a matter of lifting and shutting a lid as was commonly believed," says Professor Vandenberg.

The team suspects this 'gate mechanism' will also apply to other channels that are important in the heart's electrical system, as well as those that control electrical communication in the brain.

"The biggest benefit of this research is that it should allow the better

design of drugs so they no longer block these important electrical channels in the heart," added Professor Vandenberg. "In time, this should allow patients the freedom and peace of mind to take their medication without the fear of their heart suddenly stopping."

Provided by Research Australia

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