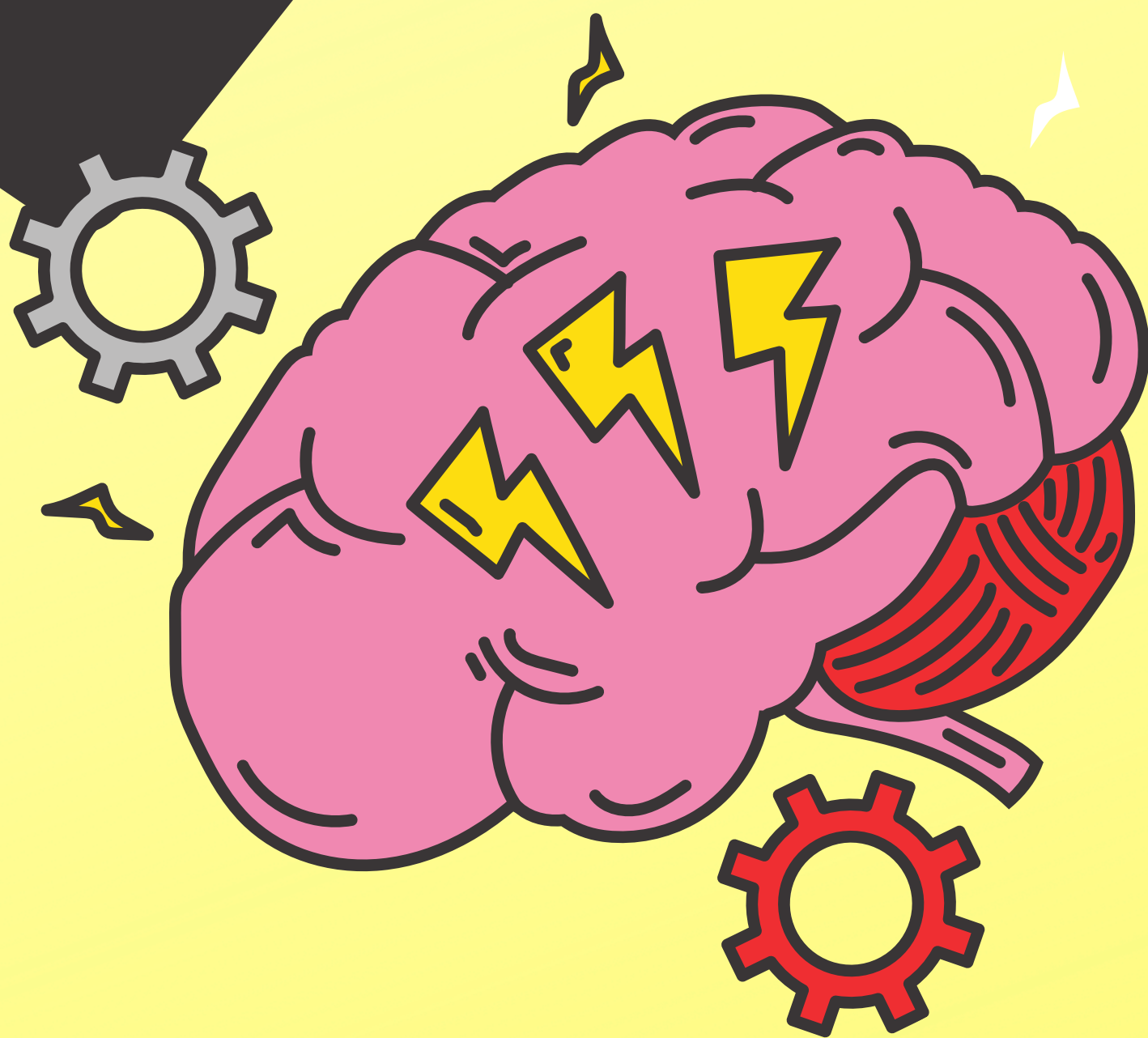
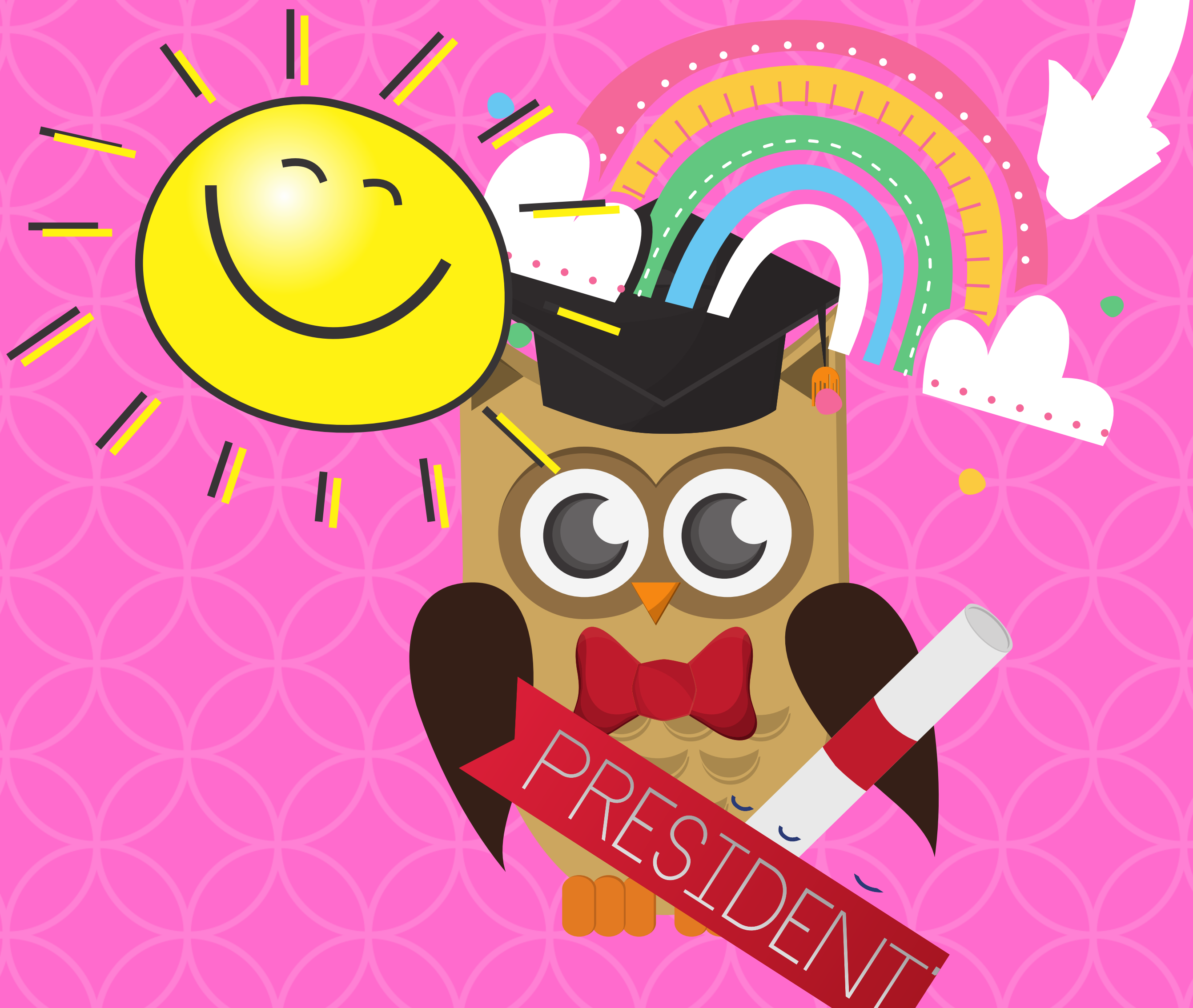


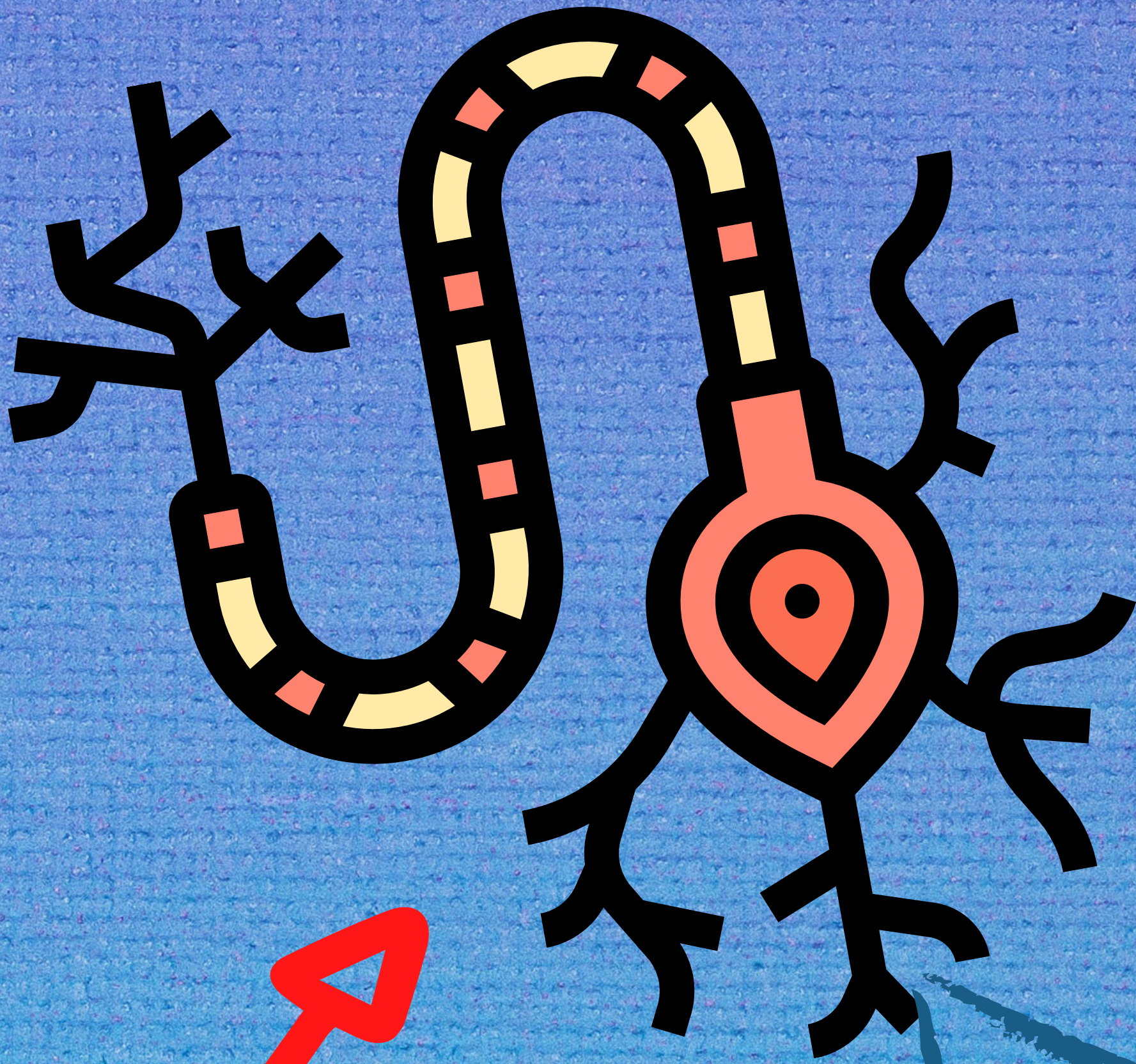
WHY DOES CAFFEINE KEEP ME AWAKE?



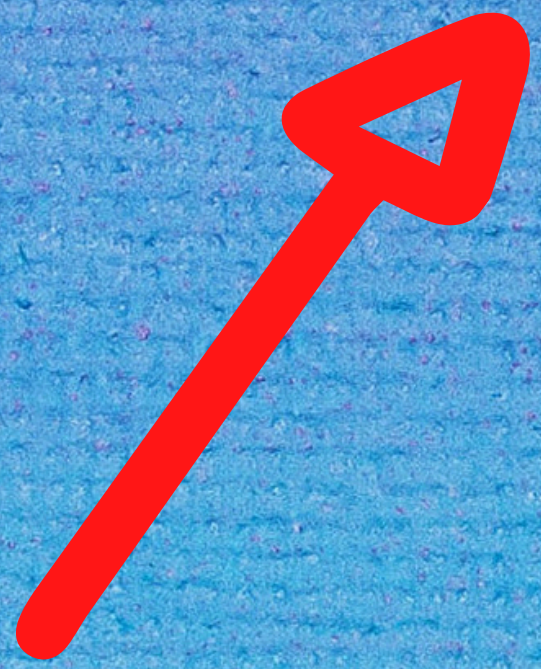
SUPER SIMPLE GUIDE



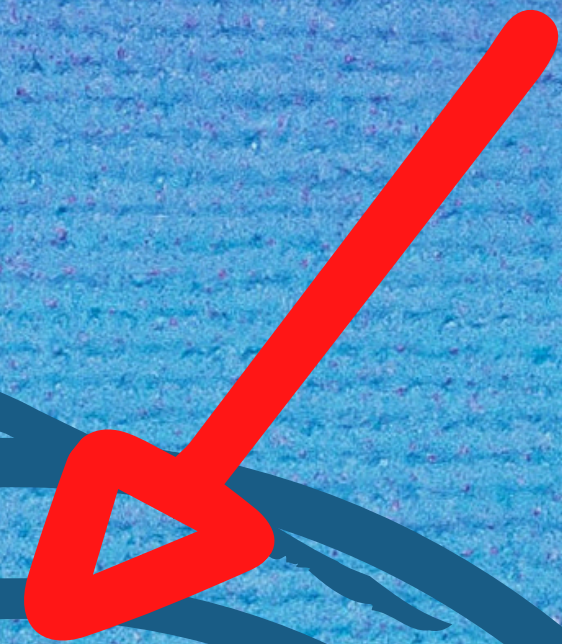




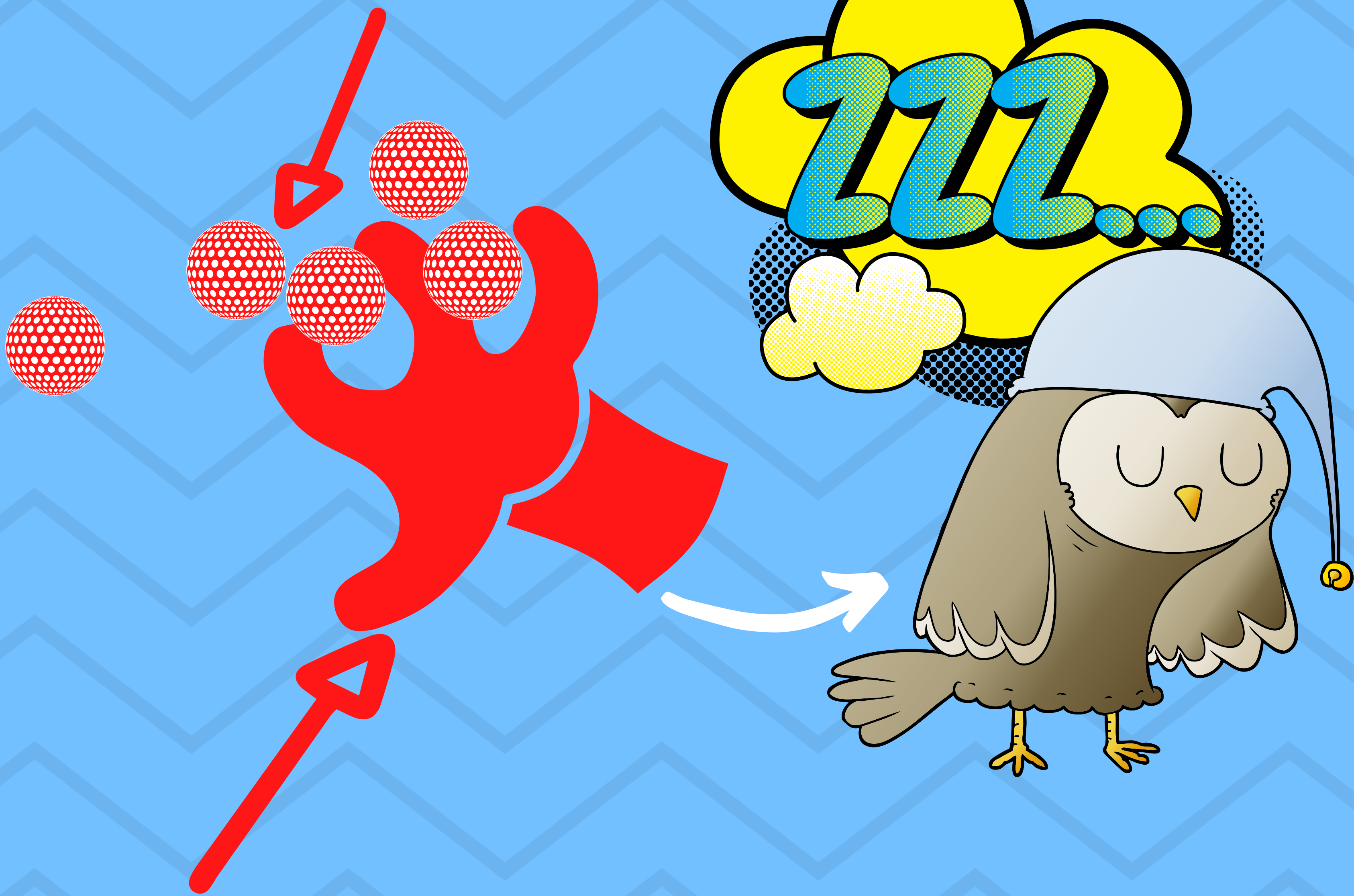
**Adenosine
receptors**



Brain cell



Adenosine

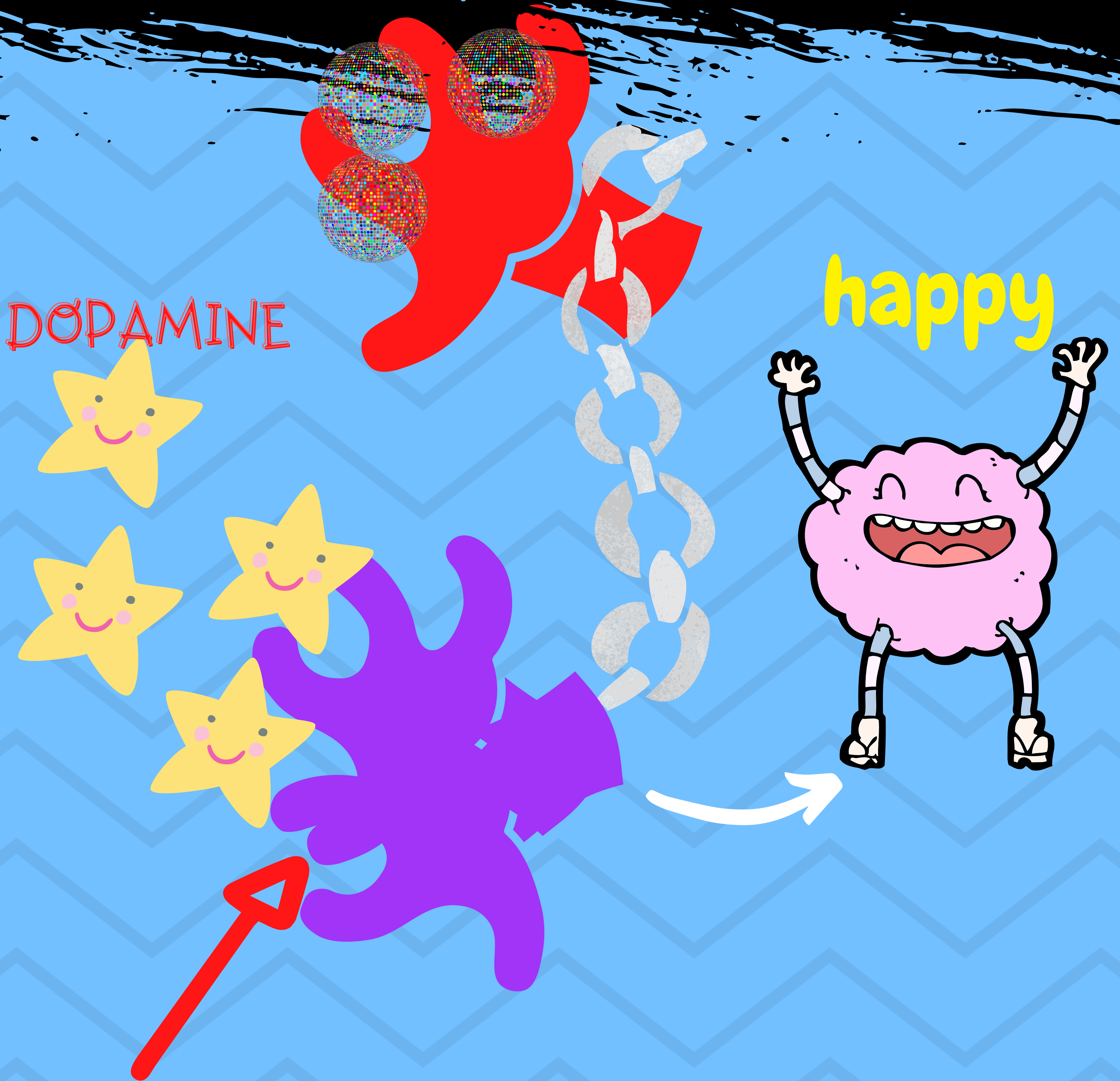


Adenosine receptor



CAFFEINE BLOCKS THE
RECEPTOR SO ADENOSINE
CANNOT ACTIVATE IT
AND MAKE US SLEEPY

LINKED TO THE DOPAMINE RECEPTOR, AND FREES UP MORE SPACE FOR 'HAPPY' DOPAMINE (RECEPTOR AVAILABILITY)





ADENOSINE RECEPTORS
MAKES US SLEEP



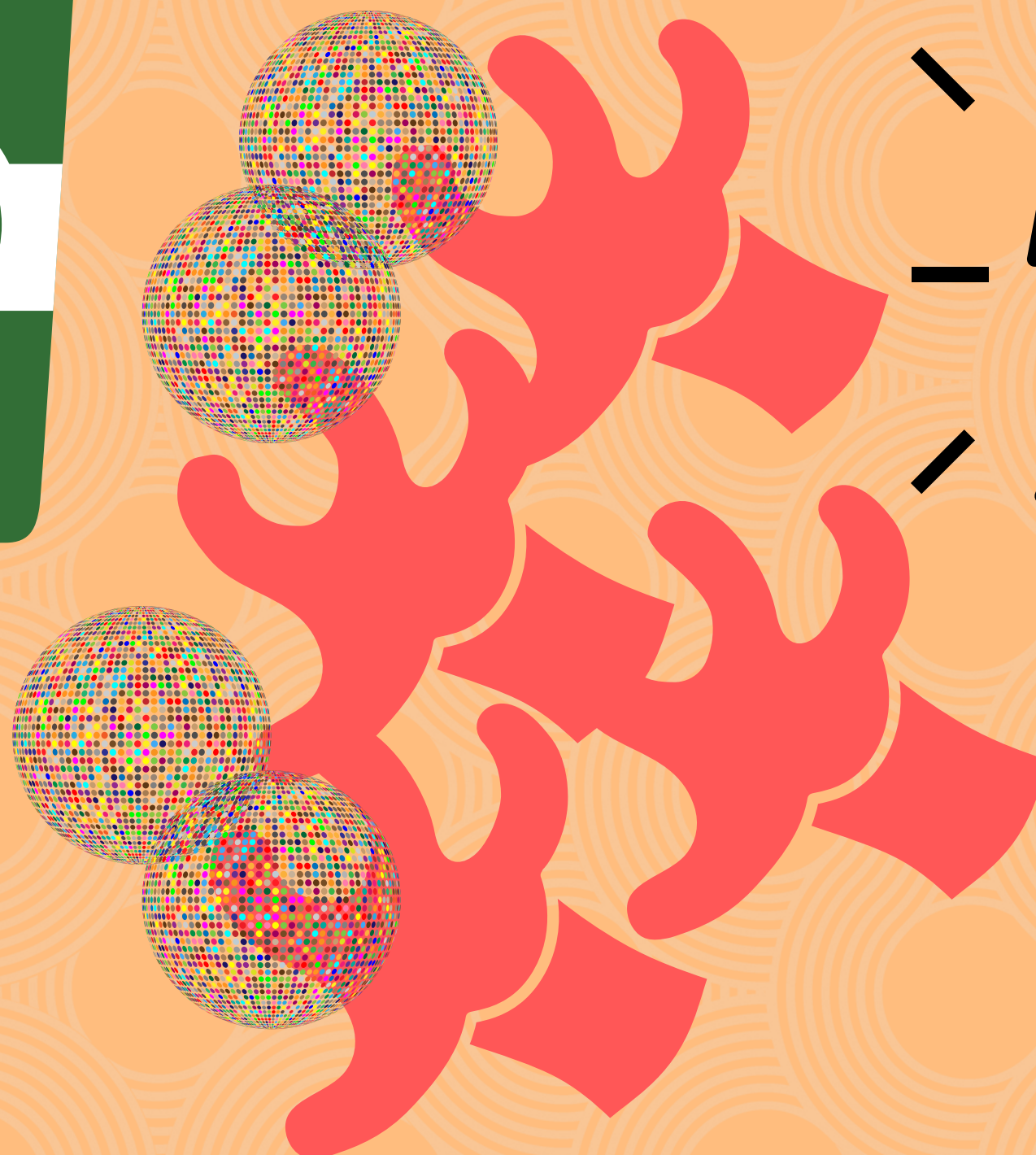
BLOCKING ADENOSINE
MAKES US FEEL AWAKE
AND MAYBE HAPPIER



CAFFEINE BLOCKS ALL
ADENOSINE RECEPTORS
(A1, A2A, A2B, A3)

HOWEVER.....

OUR BRAIN CELLS ADAPT,
AND SO WE NEED MORE
COFFEE OVER TIME



HARDCORE SCIENCE TIME

Caffeine is in the class of xanthine compounds, and we all know that it can be used as a stimulant. Most of the effects are studied on the Adenosine receptors, subtypes A1, A2a, although it is now known that caffeine works on all subtypes (A2b, A3). Caffeine works by blocking the adenosine receptors, but not activating them (competitive antagonist). It keeps us awake because adenosine is important in making us feel tired. Adenosine builds up throughout the day and signals that it is time for sleep.

A1 receptors are all over the brain and found in the highest concentrations in the cerebral and cerebellar cortices, hippocampus, and thalamic regions. Pre-synaptic A1 receptors generally inhibit neurotransmitter release.

A2a receptors are often co-localised with dopamine receptors (D2-like). Blockade of A2a receptors in the basal ganglia (corpus striatum & globus pallidus) are the most important for the stimulatory effect of caffeine.

It is thought that dopamine involvement increases when we take caffeine as adenosine normally inhibits A2a receptors, which, through intracellular 2nd messenger systems alter dopamine binding. Therefore, caffeine increases dopamine receptor availability likely by changing the receptor shape or function, thereby increasing dopamine binding and feeling goooooood. The body builds a tolerance to caffeine by upregulating the adenosine receptors, so you need more caffeine to block them all.

A good paper about adenosine/dopamine heteromers is Volkow, 2015, *Transl Psych*, 5, e549