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ATPergic signalling during seizures and epilepsy

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## ACCEPTED MANUSCRIPT

1	ATPergic signalling during seizures and epilepsy
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6	
7	Abstract:
8	Much progress has been made over the last few decades in the identification of new anti-epileptic drugs
9	(AEDs). However, 30% of epilepsy patients suffer poor seizure control. This underscores the need to
10	identify alternative druggable neurotransmitter systems and drugs with novel mechanisms of action. An
11	emerging concept is that seizure generation involves a complex interplay between neurons and glial
12	cells at the tripartite synapse and neuroinflammation has been proposed as one of the main drivers of
13	epileptogenesis. The ATP-gated purinergic receptor family is expressed throughout the brain and is
14	functional on neurons and glial cells. ATP is released in high amounts into the extracellular space after
15	increased neuronal activity and during chronic inflammation and cell death to act as a neuro- and
16	gliotransmitter. Emerging work shows pharmacological targeting of ATP-gated purinergic P2 receptors
17	can potently modulate seizure generation, inflammatory processes and seizure-induced brain damage.
18	To date, work showing the functional contribution of P2 receptors has been mainly performed in animal
19	models of acute seizures, in particular, by targeting the ionotropic P2X7 receptor subtype. Other
20	ionotropic P2X and metabotropic P2Y receptor family members have also been implicated in
21	pathological processes following seizures such as the P2X4 receptor and the P2Y12 receptor. However,
22	during epilepsy, the characterization of P2 receptors was mostly restricted to the study of expressional
23	changes of the different receptor subtypes. This review summarizes the work to date on ATP-mediated
24	signalling during seizures and the functional impact of targeting the ATP-gated purinergic receptors on
25	seizures and seizure-induced pathology.
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