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大鼠脑活性阿片结合蛋白——一种含有甘露糖基的糖蛋白[1]

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提要　大鼠脑活性阿片结合蛋白借助三齿草藤凝集素(VBL)获得部分纯化。活性阿片结合蛋白由α-甲基-D-甘露糖基显示与VBL的特异性结合，证实阿片受体也含有甘露糖基，活性阿片结合蛋白经VBL柱纯化约200倍。VBL可以用作阿片受体的纯化工具，它比常用的受体纯化试剂麦胚凝集素(WGA)更好。

关键词　内啡肽受体；载体蛋白；凝集素

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兔脑室注射山黄若碱引起发作性放电的作用部位及安定的拮抗作用[1]

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Sites of seizure discharges after intracerebroventricular injection of anisodamine and the antagonism by diazepam in rabbits[1]

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ABSTRACT　Anisodamine is a tropine alkaloid isolated from *Scopolia tangutica Maxim*. To determine the original sites of anisodamine seizure discharge, permanent electrodes were implanted into different parts of the brain in rabbits and the electrical activities were continuously recorded by monopolar leads. Injection of anisodamine 1.5 mg/kg into the lateral ventricle of conscious rabbits always produced abnormal discharges. The spike discharges

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appeared first in the amygdala and consisted of rhythmic large surface-positive spikes. Multiple spikes then appeared in the *hippocampus, caudate nucleus, midbrain* reticular formation and frontal cortex.

Diazepam 1.5-2.5 mg/kg did not inhibit the spike discharges from the amygdala, but did inhibit the discharges from other sites as well as clonic convulsions. When the dosage of diazepam was increased to 4.5 mg/kg, the spike discharges from the amygdala were also inhibited.

The above findings indicate that the site of origin of anisodamine seizure discharges in rabbits is the amygdala. The seizure discharges then spread to the mesencephalic reticular formation, the hippocampus, the caudate nucleus and the cortex. Diazepam was shown to be an effective *antagonist against central stimulation* induced by anisodamine.

KEY WORDS anisodamine; diazepam; amygdaloid body; implanted electrodes; electroencephalography; atropine derivatives

提要 清醒兔 icv 山莨菪碱 1.5 mg/kg, 5-30 min 后首先在杏仁核出现有规律的向下的单个棘波放电，尔后在海马、尾核、中脑网状结构和大脑皮层出现连续棘波放电。提示 icv 山莨菪碱引起发作性放电的作用部位为杏仁核。iv 安定 1.5-4.5 mg/kg 显著抑制山莨菪碱引起的棘波放电及运动性惊厥。

关键词 山莨菪碱；安定；杏仁核；埋藏电极；脑电描记术；阿托品衍生物

山莨菪碱(anisodamine)系从唐古特山莨菪(*Scopolia tangutica* Maxim)分离的生物碱。作者等曾报道 icv 山莨菪碱可以引起兔 EEG 发作性放电及运动性惊厥[1]，但是对引起 EEG 发作性放电的作用部位尚未见报道。本文通过在兔同侧额或枕部皮层、海马、杏仁核、尾核以及中脑网状结构植入慢性埋藏电极，单极记录电活动，然后在同侧 icv 山莨菪碱。根据棘波放电出现的先后次序，判断放电作用的原发部位，并观察了安定对山莨菪碱作用的影响。

MATERIALS AND METHODS

兔 25 只，体重 2.25±SD 0.30 kg，♀♂兼用。在戊巴比妥钠麻醉下进行埋藏皮层下电极的手术。采用经常规绝缘处理的不锈钢丝(φ 0.3 mm)电极，埋藏后用牙托粉固定。皮层下结构的定位参考 Sawyer 等兔间脑定位图谱[2]，海马(P_4, L 或 R_4, H_5)，杏仁核(A_{2-3}, L 或 R_6, H_{-4})，尾核(APO, L 或 R_6, H_4)，中脑网状结构(P_8, L 或 $R_{2.5}$, H_{-2})。术后 5-7 d 进行实验。皮层、皮层下结构生物电活动记录方法以及 icv 部位同前文[1,3]，用 SJ-42 型多导生理记录仪记录。每侧 icv 药物容量 0.1 ml，耳缘静脉 iv。以兔脑生物电和行为(不安、惊厥)的变化为观察指标。实验结束后用普鲁士蓝法验证电极植入的部位。

氢溴酸山莨菪碱(青海制药厂生产)，用生理盐水配制。安定(diazepam)，上海第十三制药厂生产，注射用针剂原液。

RESULTS

清醒兔给药前在安静环境中，额部皮层、杏仁核、中脑网状结构等部位的电活动为 40-150 μV 的 θ 节律，海马电活动为 6 cps 波幅 150-400 μV 的海马节律。icv 山莨菪碱 1.5 mg/kg, 5-30 min 后，首先在杏仁核出现间歇的规律的单个棘波(波幅 800 μV)放电。48 min 后，皮层、杏仁核、海马和中脑网状结构同步出现连续棘波放电，动物出现阵挛性惊厥，持续约 30 s。连续放电停止后间隔较长一段时间(13 s)，先在杏仁核恢复单个棘波放电，尔后在皮层、海马和中脑网状结构出现与杏仁核同步的或非同步的单棘波放电，作用持续 60 min 以上(Fig 1)。埋藏有尾核电极的 3 只兔中，尾核棘波放电亦是随杏仁核之后出现。icv 山莨菪碱后，兔均出现呼吸急促、颤抖、面肌抽搐、眼睑跳动、眼球震颤和对触摸敏感等高度兴奋现象，尔后出现全身阵挛性惊厥。连续棘波放电与惊厥发作之间不完全同步，有

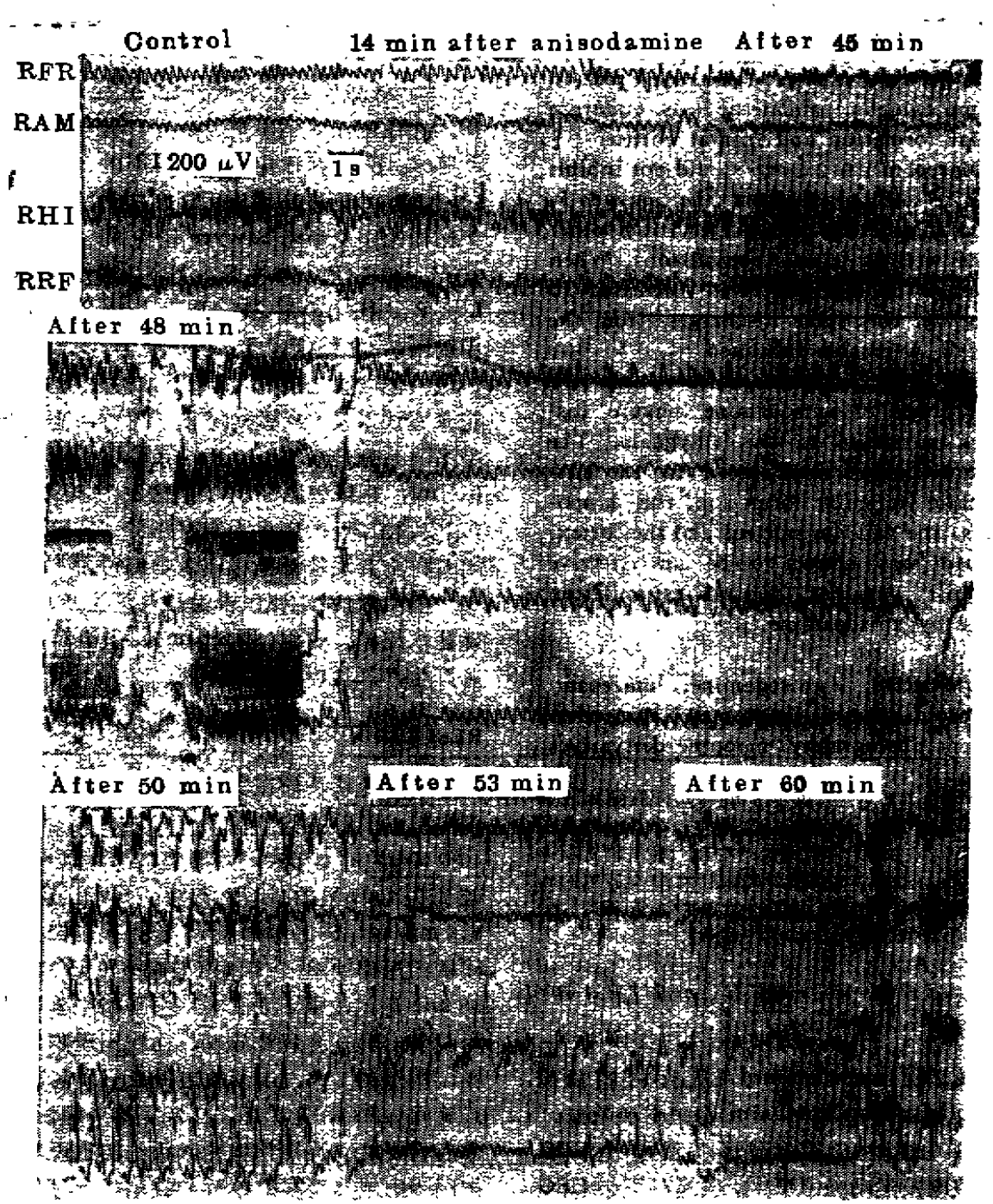

Fig 1. The EEG activity of the cortex, amygdala, hippocampus and midbrain reticular formation on the right brain in a conscious rabbit after injection of anisodamine 1.5 mg/kg into the right lateral ventricle. The spike discharges appeared first in the amygdala 14 min after anisodamine. About 48 min after injection, all EEG leads exhibited multiple spikes and rhythmic spike waves continued for at least 60 min. RFR = right frontal; RAM = right amygdala; RHI = right hippocampus; RRF = right midbrain reticular formation.

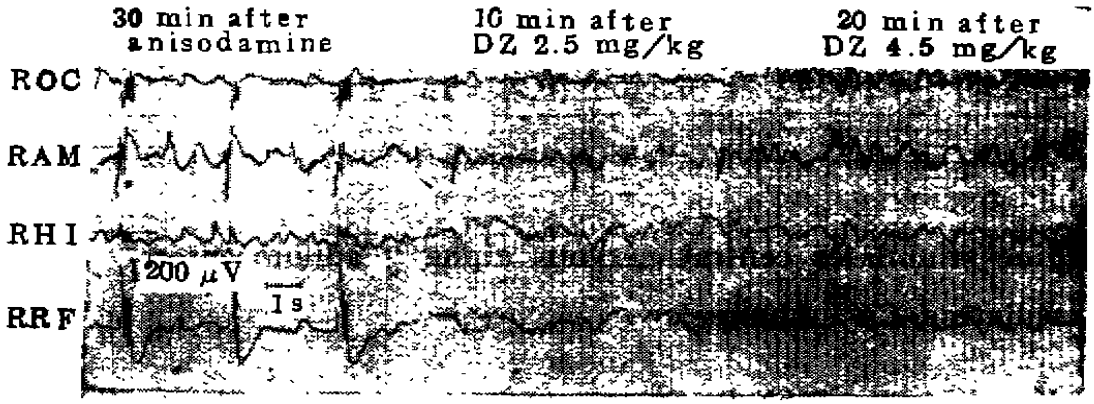

Fig 2. Diazepam (DZ) antagonism of anisodamine-induced abnormal discharges of EEG activation. EEG spike waves were present 30 min after icv 1.5 mg/kg of anisodamine. 10 min later, DZ (2.5 mg/kg iv) did not inhibit the spike discharges from the amygdala, but inhibited the discharges from other sites. 20 min after DZ 4.5 mg/kg inhibited the spike discharges in all of leads. ROC = right occipital; RAM, RHI and RRF as the same in Fig 1.

时 EEG 出现连续棘波放电，但兔无阵挛性惊厥。

在 icv 山莨菪碱兔出现棘波放电 30 min 后，iv 安定 1.5–2.5 mg/kg 不能完全抑制杏仁核棘波放电，但能抑制其它部位的放电，消除兴奋现象及抑制惊厥发生。安定增加至 4.5 mg/kg 时，杏仁核棘波放电亦被抑制 (Fig 2)。

DISCUSSION

实验证明兔 icv 山莨菪碱引起发作性放电的原发部位为杏仁核，而后波及中脑网状结构、海马、尾核和大脑皮层。对于山莨菪碱中枢兴奋作用的性质，作者等曾认为与 GABA 能神经因素有关[1]。Soubrie 等根据中枢抗胆碱药引起的小鼠活动增多可被安定拮抗，认为可能包含 GABA 机理[4]。本实验证明安定有显著抑制山莨菪碱引起的惊厥及发作性放电作用。现已证实杏仁核和海马等边缘系统含有丰富的苯二氮䓬类受体[5]，安定抗山莨菪碱作用可能是与杏仁核内苯二氮䓬受体结合，加强中枢抑制性 GABA 能神经功能的结果。

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