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Research Report

The α2 adrenoreceptor agonist clonidine suppresses evoked and spontaneous seizures, whereas the α2 adrenoreceptor antagonist idazoxan promotes seizures in amygdala-kindled kittens

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ABSTRACT

Microinfusion of α2 adrenoreceptor agonists and antagonists into amygdala has contrasting effects on evoked and spontaneous seizure susceptibility in amygdala-kindled kittens. Subjects were 14 preadolescent kittens between 3 and 4 months old at the beginning of kindling. The same protocol was followed except that half the kittens received microinfusions (1 μl) of the α2 agonist clonidine (CLON; 1.32 nmol), and half received the α2 antagonist idazoxan (IDA; 0.33 nmol). Infusions were made over 1 min through needles inserted into cannulae adjacent to stimulating electrodes in the kindled amygdala, and evoked seizures were tested 10–12 min later. The results were: (1) CLON elevated seizure thresholds obtained once at the beginning and end of kindling, but only when compared to sham control values (needle insertion only) in the same animals; IDA significantly reduced thresholds. (2) CLON retarded and IDA accelerated kindling rate, defined as the number of afterdischarges (ADs) required to achieve the first stage 6 seizure or generalized tonic–clonic convulsion (GTC). These effects were most pronounced on the emergence of seizure "generalization" stages (3–6) from "focal" seizure stages (1–2). (3) CLON prevented onset of spontaneous seizures, whereas IDA precipitated onset of spontaneous seizures in 100% of the animals before or during the 5-week post-kindling follow-up during which seizures were evoked once each work day. The study confirms previous findings in kindled rodents to show that CLON and IDA can have opposing effects on kindling development in kittens and is the first report to show contrasting effects on spontaneous epileptogenesis in kindled animals as well.

1. Introduction

Norepinephrine (NE) has well documented antiepileptic effects in various experimental epilepsy models (Applegate et al., 1986; Barry et al., 1989; Bjorklund and Lindvall, 1989; Bengzon et al., 1991; Boyajian and Leslie, 1987; Browning et al., 1989; Callaghan and Schwark, 1979; Corcoran, 1988; Corcoran and Mason, 1980; Corcoran et al., 1976; Gellman et al., 1987; McIntyre and Edson, 1989; Pelletier and Corcoran, 1993; Shouse, 2004; Shouse et al., 1994, 1996; Tacke and Kolonen, 1984; Weiss et al., 1990),

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including amygdala kindling (Applegate et al., 1986; Barry et al., 1989; Callaghan and Schwark, 1979; Corcoran, 1988; Corcoran and Mason, 1980; Engel et al., 1978; Gellman et al., 1987; McIntyre and Edson, 1989; McIntyre and Guigna, 1988; Pelletier and Corcoran, 1993; Shouse et al., 1990, 1994, 1996, 2001, 2004). The α2 adrenoreceptor is thought to be the most influential site of action (Pelletier and Corcoran, 1993). Microinfusion of noradrenergic agonists and antagonists into the amygdala have opposing effects on amygdala kindling development in adult rats (Pelletier and Corcoran, 1993) and on post-kindling seizure thresholds in kittens (Shouse et al., 1996). This report confirms and extends previous findings by showing that the α2 noradrenergic agonist clonidine (CLON) not only elevates seizure thresholds in kittens but also retards the development of kindling, as indexed by the number of evoked afterdischarges (ADs) required to achieve the first stage 6 seizure, when compared to effects of the α2 adrenoreceptor antagonist idazoxan (IDA). To our knowledge, this is the first report

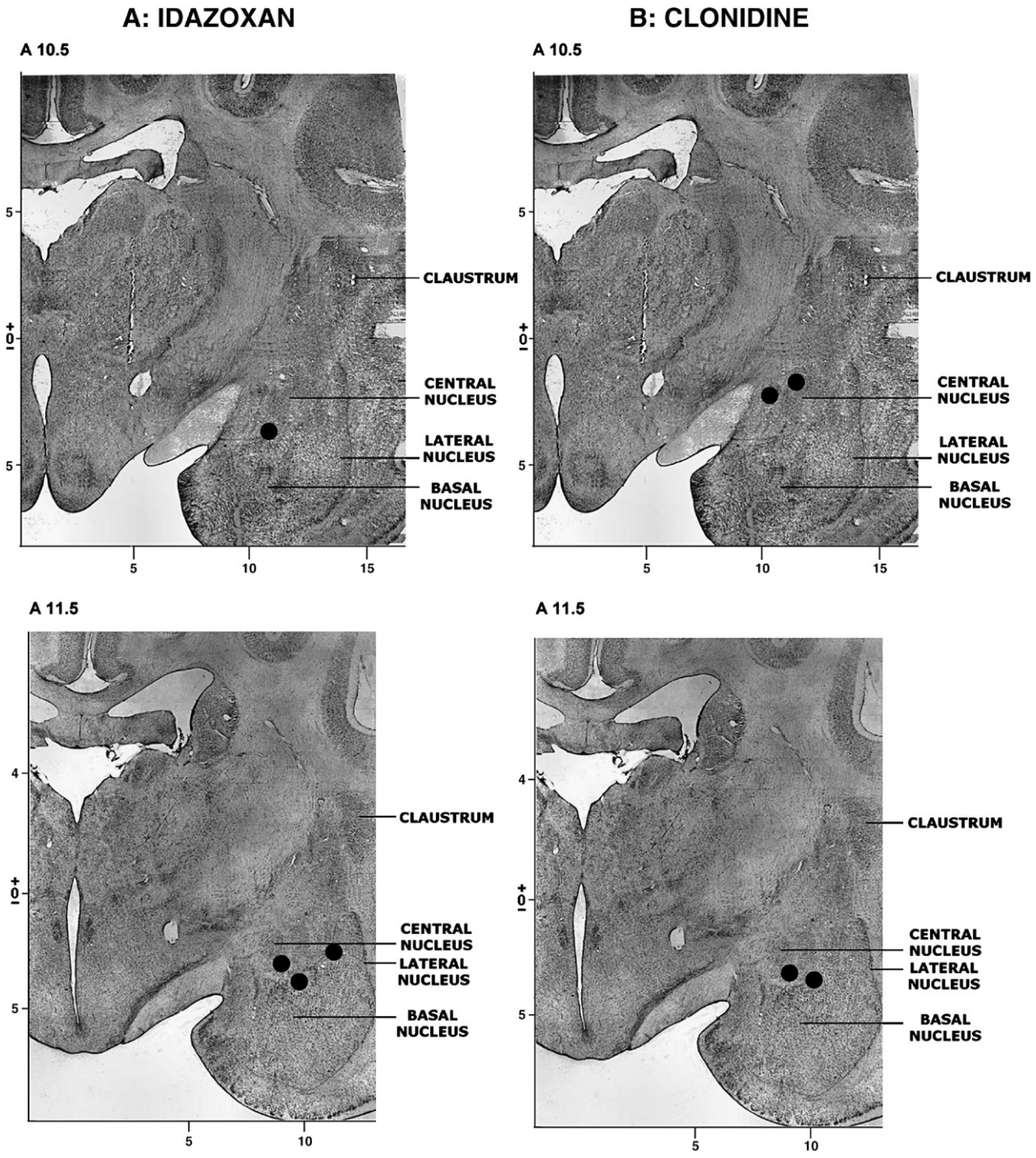

Fig. 1 – Location of amygdala kindling electrodes in 14 animals based upon assignment to the idazoxan (A: *n*=7) or the clonidine (B: *n*=7) microinfusion groups. Coronal sections are from anterior or A10.5–13.0 from the Snider and Niemer atlas (Shouse et al., 2001). Circles=right hemisphere (*n*=13); triangle=left hemisphere (*n*=1).