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Research Report

Effects of electroacupuncture on retinal nerve growth factor and brain-derived neurotrophic factor expression in a rat model of retinitis pigmentosa

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ABSTRACT

The aim of this study was to investigate the effect of electroacupuncture (EA) on the progression of retinal degeneration in rats affected by inherited retinitis pigmentosa (IRP) and to correlate this event with the retinal expression of neurotrophins. Thirty-day-old Royal College of Surgeons (RCS) rats were exposed to 25-min-long daily sessions of low-frequency EA for 11 consecutive days. Control-untreated and EA-treated rats were sacrificed 1 h after the last EA session, and their retina removed for biochemical, molecular, and immunohistochemical analyses. Our data revealed that daily sessions of low-frequency EA for 11 days to RCS rats during a critical developmental stage of retinal cell degeneration cause an increase of retinal nerve growth factor (NGF) and NGF high-affinity receptor (TrkA) expression; and increase of outer nuclear layer (ONL) thickness; and enhanced vascularization. These findings suggest the possible beneficial effects of EA treatment in the development of IRP-like retinal degeneration of RCS rats and that the mechanism through which EA might exerts its action on the regulation of NGF and brain-derived neurotrophic factor (BDNF) and/or their receptors in retinal cells.

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Abbreviations:
NGF, nerve growth factor
BDNF, brain-derived neurotrophic factor
VEGF, vascular endothelial growth factor
RCS, Royal College of Surgeons
IRP, inherited retinitis pigmentosa
GC, ganglion cell
INL, inner nuclear layer
IPL, inner plexiform layer
ONL, outer nuclear layer
RPE, retinal pigment epithelium
CNS, central nervous system
EA, electroacupuncture
UT, untreated
PCO, polycystic ovary syndrome
TrkA, tyrosine-kinase A
TrkB, tyrosine-kinase B
SD, Sprague–Dawley

1. Introduction

Nerve growth factor (NGF) is one of the most extensively studied neurotrophic factors produced and released by numerous mammalian cells, such as neuronal, epithelial, endothelial, endocrine, and immune cells (Aloe et al., 2001; Levi-Montalcini, 1987; Sofroniew et al., 2001). NGF is produced by cells of the visual system, and NGF receptors are express by retinal pigment epithelium (RPE), Muller cells, retina ganglion cells (GC), and by photoreceptor (Amendola and Aloe, 2002; Amendola et al., 2003; Carmignoto et al., 1989; Lambiase et al., 1998; Lambiase et al., 2005; Siliprandi et al., 1993). It has been shown that the intraocular administration of NGF protects from retinal GC degeneration after optic nerve transection, ocular ischemia, or experimentally induced ocular damage, thus suggesting a functional role of NGF in the visual system (Carmignoto et al., 1989; Siliprandi et al., 1993). Moreover, ocular NGF administration is able to delay retinal degeneration in animal models of inherited retinitis pigmentosa (IRP), in CH-3 mouse strain (Lambiase and Aloe, 1996), and in Royal College of Surgeon rat (RCS). NGF retrobulbar injection, aimed at stimulating NGF-receptive sites in the retina, is considered an invasive approach because it can produce undesired side effects. Recent studies indicate that it is possible to stimulate endogenous release of NGF both in the peripheral (Stener-Victorin et al., 2000) and in central nervous system (CNS) (Stener-Victorin et al., 2003) by electroacupuncture (EA). EA is a therapeutic method based on the ancient Chinese treatment for illness, pain, or even addiction, which uses fine needles inserted in specific points of the body. Studies published in the last few years indicate that EA can affect neurological and non-neurological disorders. However, the possible biochemical and molecular mechanisms through which EA exerts its effect remain undefined. It has been suggested that low-frequency (1–4 Hz) EA with repetitive muscle contraction results in the activation of physiological processes similar to those resulting from physical exercise (Andersson and Lundeberg, 1995). There is also evidence indicating that EA stimulates the release of different neurotransmitters, both in the CNS and in the peripheral nervous system (PNS) (Bucinskaite et al., 1994; Jansen et al., 1989), and that it can modulates immunological responses and the release of cytokines (Gronlund et al., 2004; Smith et al., 2004). It has also been reported that EA can affect the concentration of NGF in a rat model of polycystic ovaries (PCO) (Stener-Victorin et al., 2000; Stener-Victorin et al., 2003; Yun et al., 2002), in the CNS (Liang et al., 2002), and in the visual system (Chan et al., 2005; Chu and Potter, 2002; Dabov et al., 1985; Smith et al., 2004; Uhrig et al., 2003; Ulett et al., 1997). These observations raised the question of whether EA can influences the presence of neurotrophins and their receptors in the retina of rats affected by IRP. To address this question, we exposed RCS rats to daily sessions of EA during a critical period of retinal degeneration, and the biochemical, structural, and molecular responses of NGF and BDNF in the retinal tissues were examined.

2. Results

2.1. *General observations*

Daily exposure of RCS rats to low-frequency EA at 2 Hz for 11 consecutive days does not affect recovery time from anesthesia and causes no changes in other behavioral manifestations, such as feeding behavior, social behavior with littermates, and body weight.

2.2. *Effect of EA on NGF and NGF receptors*

Fig. 1 shows the expression of NGF protein (Fig. 1A) and its mRNA (Fig. 1B) in the retina of RCS rats exposed to daily EA session for 11 consecutive days. The expression of NGF and NGF mRNA in the retina of EA-treated RCS rats is higher compared to that of age-matched RCS-untreated (UT) rats.