greater incidence of glaucomatous damage than other musicians, which was related to life hours of playing. The authors speculated that the cumulative effects of long-term intermittent IOP elevations during high resistance wind instrument playing might result in glaucomatous damage.

Based on the above research findings and Valsalva hypothesis of AD, extensive use of the VM could be suggested as a possible common risk factor for both NTG and AD. The present author, therefore, hypothesises the presence of a subset of NTGs who may exhibit AD-related pathology due to frequent performance of the VM, predisposing to both disorders. It could be speculated that excessive Valsalva might be causally related to both NTG and AD through hemodynamic alterations. In healthy subjects, it has been shown that the pulsatile ocular blood flow is significantly reduced during Valsalva and is proportional to the elevation of intrathoracic pressure [5]. Additionally, Pott et al. [6] found that, particularly in the upright posture, straining against a closed glottis may critically compromise cerebral perfusion. Such hemodynamic alterations are in agreement with the currently prevailing concept of vascular involvement in the pathogenesis of both glaucoma and AD [7,8]. With regard to AD, epidemiological studies show that practically all risk factors reported thus far have a vascular component that reduces cerebral perfusion [8].

It should be stressed, however, that it may be possible to hypothesise other common etiologic factors and pathologic mechanisms that might also exist for both NTG and AD, at least in some patients.

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# Targeting cerebral Bcl-2 expression as a potential therapeutic target in autism: Potential usefulness of human recombinant nerve growth factor

*Dear Editor,*

A growing body of evidence has clearly indicated that abnormalities in the neuronal apoptotic pathways may play a significant role in the pathogenesis of autistic spectrum disorder (ASD) [1]. Accordingly, a reduced level of expression of the anti-apoptotic protein Bcl-2 has been consistently demonstrated in the frontal, parietal, and cerebellar cortices of ASD patients [2—4]. In the light of these findings, it would be tempting to speculate that stimulation of Bcl-2 expression in the central nervous system may be a potential therapeutic target in autism and related neurodevelopment disorders.

We propose that such an effect on cerebral Bcl-2 levels could be achieved via administration of human recombinant nerve growth factor (hrNGF).

Accordingly, preliminary *in vitro* data have shown that treatment with nerve growth factor may greatly enhance the level of Bcl-2 expression in cultured neurons, thereby resulting in enhanced neuronal survival and reduced vulnerability to apoptotic cell death [5].

Since previous human studies have clearly demonstrated that delivering of hrNGF is safe and generally well tolerated in doses up to 1.0 μg/kg when given intravenously or subcutaneously [6], we believe that clinical trials aiming to investigate the clinical effectiveness of hrNGF on the core symptom domains of autism would be highly desirable. Alternatively, investigations on the possible effects of hrNGF administration on the cerebral expression of Bcl-2 protein as well as on behavioural phenotypes in existing animal models of ASD would also be feasible prior to testing this therapeutic approach in human clinical studies.

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# Cytosine deaminase producing *Clostridium* may be used in detection of tumors

Hypoxia and anoxia are pathophysiologic characteristics of most solid tumors [1] and provide a niche for anaerobic bacteria. Various types of non-pathogenic obligate anaerobic and facultative anaerobic bacteria have been shown to infiltrate and selectively grow within solid tumors when delivered systemically [2]. For example, after systemic administration of non-pathogenic clostridia, these strictly anaerobic, spore-forming bacteria give a selective colonization of hypoxic/necrotic areas within the tumors [3]. In addition, some recombinant *Clostridium* strains can produce cytosine deaminase, which converts the non-toxic 5-fluorocytosine (5-FC) to the toxic 5-fluorouracil (5-FU), and used in clostridial-directed enzyme prodrug therapy (CDEPT) [4].

The fluorine atom provides an exciting tool for diverse spectroscopic and imaging applications using magnetic resonance [5]. Magnetic resonance spectroscopy (MRS) has been used as an effective and non-invasive method for specifically monitoring *in vivo* expression of the cytosine deaminase in transgenic human tumors, because 5-FC and its major metabolites are fluorinated and $^{19}F$ produces a strong MRS signal with no background from endogenous compounds. This quantitative assessment does not require blood sampling, because the concentrations of the precursor can be directly and simultaneously measured in the tissue [6].

We proposed that cytosine deaminase producing *Clostridium* can be used in detection of tumors with MRS. Since mammalian cells lack cytosine