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Artículo:

Music alters constitutivety expressed opiate and cytokine processes in listeners Is it possible to restore function with two percent surviving neural tissue? Basic concepts of neuroepidemiology and statistic Late post-acute neurologic rehabilitation: neuroscience, engineering and clinical programs

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Music alters constitutively expressed opiate and cytokine processes in listeners

Summary

Background: Listening to music as a means of inducing a sense of calm and relaxation has been known for some time.

Although these effects are robust, little research has been conducted into exploring the underlying neurochemical changes, which must occur to provide an individual with these objective sensations.

Material/methods: In the current report we utilize an AB design to explore observed differences in blood plasma signaling molecules in pre- and post music listening groups when compared with controls.

We focus chiefly on cytokines, as well as peripheral blood mononuclear cells and polymorphonuclear cells.We utilized reverse transcription followed by real-time polymerase chain reactions to determine relative mRNA expression for the mu opiate receptor gene.

Using high pressure liquid chromatography coupled to electrochemical detection as well as nano electrospray ionization double quadrupole orthogonal acceleration time of flight-mass spectrometry we determined opiate alkaloid levels.

Results: Our findings are two-fold: with regard to mu opiate receptor expression, mononuclear cells showed a statistically significant increase in subjects in the music group compared to the control.

Plasma morphine levels were found to be non-significantly lower in subjects after listening to music when compared to control subjects whereas morphine 6 glucuronide levels increased slightly, suggesting morphine's conversion to morphine 6 glucuronide. IL- 6 levels were significantly lower as well whereas IL-1b, IL-10 and cortisol values were unchanged.

Conclusions: Taken together, it appears that music-listeners exhibit plasma signal molecule changes consistent with the physiological changes associated with the reported actions of music, i.e, lower blood pressure.

Key words: Music, music therapy, opiate, morphine, morphine 6 glucuronide, interleukin-6, mu opiate receptors, complementary medicine, monocytes, cytokines.

Listening to music as a means of inducing a sense of calm and relaxation has been known for some time. Although these effects are robust, little research has been conducted into exploring the underlying neurochemical changes, which must occur to provide an individual with these objective sensations. Taken together, it appears that music-listeners exhibit plasma signal molecule changes consistent with the physiological changes associated with the reported actions of music, i.e, lower blood pressure.

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Is it possible to restore function with two percent Surviving neural tissue?

How much surviving normal neural tissue is required for functional reorganization after a lesion? Clinical and experimental studies suggest that at little as two percent remaining tissue may be sufficient, at least in some cases, for functional reorganization. Recent sensory substitution studies with persons who have been diagnosed with total vestibular loss (e.g., due to an toxic reaction to an antibiotic) suggest that the persisting function after removal of the substitution system may be related to the survival of a small amount of vestibular tissue.

Key words: Brain plasticity, functional reorganization, stroke, vestibular loss, brain damage.

A recent study reported in this Journal[9] demonstrated persisting function after a period of use of a vestibular substitution device.The therapeutic effect demonstrated by research subjects strongly suggests the persistence of a small amount of surviving vestibular sensory tissue.This re-opens a question regarding the percentage of neural tissue required to restore function after brain or neural tract damage.

Previous studies suggest that as little as 2 percent of surviving neural tissue in a system can serve as the basis for functional reorganization.The following is an excerpt from,[3] pp. 245: \It is evident from Glees' studies on hemispherectomy[6] that reorganization of function can occur after a great amount of brain has been lost. Animal studies reveal that as little as 2% of remaining neural tissue in a particular system can mediate a high degree of function: Galambos et al[5] destroyed up to 98.5% of the optic track fibers in the cat and a few weeks after the lesions, they found almost normal visual behavior. Pattern discrimination was present and visual evoked potentials had approximately the same amplitude as pre-operatively. Previously, Lashley[7] had demonstrated that complex visual discrimination and visual behavior could be maintained in the rat if only 2% of the visual cortex remained". Some unusual cases of recovery have been reported in the past, but in the century (from approximately 1860 to 1960) in which concepts of brain plasticity were not within the conceptual substance of the neurosciences,[4] clinicians and investigators were reluctant to re-

port such findings. Almost 30 years ago,[2] (see pp. 211-212), had reported the following: "Rasmussen (personal communication) discussed the unpublished case of a man who became paraplegic following an automobile accident, but gradually regained complete function and was able to enlist in the U.S. Navy. He served three enlistment periods with no physical limitations. He died in a second automobile accident. Autopsy revealed that a complete (approximately 1 cm) separation of the spinal cord at the level of T7 had resulted from the first accident. However, microscopic study revealed approximately 150 axon cylinders embedded in the fibrous tissue separating the two portions of the spinal cord. Thus, it is likely that recovery was obtained by the functional reorganization of the input to the cell bodies of the 150 remaining fibers, as well as the possible redirection of the axon terminals".

A comparable case was published by Aguilar[1] and discussed in detail by Bach-y-Rita,[3] on pp. 238-244: it was a case that "… offered an unusual opportunity to relate brain plasticity to recovery of function following a stroke. Due to the conjunction of various factors: a cerebral vascular accident to a previously intact elderly person; an intensive therapy program; a high degree of motivation and family involvement; an excellent recovery over a period of several years; a *post-mortem* examination following death seven years after the cerebral vascular accident, from an unrelated cause".

The patient was a 65 year old college professor who returned to full time work 3 years after the event and continued to be employed until his death. He led an active life and died at age 72 of a myocardial infarction which occurred during a mountain hiking trip at an altitude of 9,000 feet. An extensive home rehabilitation program led to significant motor recovery over a 5-year period. After extensive brain damage, the functional rehabilitation apparently unmasked previously existing pathways that, prior to injury, had not had the same relationship to the recovered functions.

The damage included the destruction of the pyramidal tract, verified at autopsy 7 years later, which contained only approximately 3% of normal appearing axons scattered throughout the scar tissue, which may have been a morphological base of the functional reorganization. His home program emphasized very high patient participation in the continuing rehabilitation process.

Receptor plasticity, both at synapses and on the cell membrane away from synapses (reached by volume transmission), may play a major role in the reorganization of function after brain damage. Volume transmission may also be the principal means of neurotransmission in the noradrenergic system, which is involved in so many activities related to recovery from brain damage. Both acetylcholine and norepinephrine can provide a state of excitability consistent with cognition, which is consistent with inhibition of the locus ceruleus activity during lack of vigilance.

These findings may relate directly to the results of rehabilitation programs: when. vigilance is high and the patient is actively involved, good results are more likely to be obtained. There may also be a relationship to functional rehabilitation programs that are based on the interests of the individual patient, and to the positive results obtained with some home programs. In these cases, the increased vigilance and participation may lead to greater locus ceruleus production of noradrenaline. This and other neurotransmitter changes may also be mechanisms by which psychosocial factors influence recovery.[4]

In one extensively studied vestibular substitution subject who demonstrated residual benefits, the persistence of a sensing system should be necessary, especially since she is able to maintain balance even in a totally dark room (which eliminates the visual input) and can perform normal activities such as riding a bicycle (see web page www.brainportinfo.com). Close questioning of the subject revealed that, although she received a diagnosis of\total vestibular loss" both in her local hospital and at a national vestibular function laboratory, she was minimally nauseated at the end of a Barany chair rotation test. This suggests the persistence of at least a small amount of vestibular system tissue; it may be enough for the results obtained after the end of the vestibular substitution sessions.

Why did the therapeutic effect last for only a few seconds with a 1 minute trial or for a few hours with a 20 minute session? Following the vestibular substitution results, we postulated that in the absence of the integrated inputs to a normally closed-loop multisensory control process, an intrinsically unstable system becomes vulnerable to noise (from both internal and external sources).[9] The recordings show the dramatic effects of the open-loop control system, which is evidently suppressed for a short time by the therapeutic effect. Thus, at least in certain cases, a small amount of remaining nervous tissue may be a sufficient neural substrate. But how can this occur? One possibility is suggested by Wall's studies: unmasking (as described by Wall,[10]) may play a role in the reorganization. His experiments revealed pathways that exist in the normal state, but do not appear to function until\unmasked" by injury or temporary conduction block.

Comparably, the existence of weak non-visual inputs to cells of the cat primary visual cortex had previously been demonstrated; the responses to light were tightly grouped around a mean of 33 milliseconds in latency while those to sound and pinprick were spread out around means of 63 (sound) and 70 (pinprick) milliseconds.[8] Further, these responses to sound and pinprick were less synaptically secure, being less resistant to barbiturate narcosis than the visual responses. Studies in adult congenitally blind persons reveal that the non visual inputs to the visual cortex become prominent;[11] c.f..(4) These more tenuous pathways may be the type of masked pathways that are unmasked following neural lesion, if there is an appropriate rehabilitation or substitution program, and if there is the functional demand and the motivation to obtain the increased function.

This matter is by no means resolved, and a goal of this communications is to, stimulate discussion and research on the fascinating question of the amount of surviving neural tissue necessary for recovery of function.

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Conceptos básicos de neuroepidemiología y estadística

La importancia de la investigación en epidemiología de las enfermedades neurológicas queda manifestada en el siguiente hecho: en una revisión de Medline, tan sólo en el periodo de 1999 a 2000 aparecieron 330 referencias bibliográficas sobre el tema, cantidad de información equiparable a la de algunos padecimientos crónicos. De aquí la necesidad de conocer los conceptos básicos relacionados con el proceso de investigación. Cuando se realiza una investigación, es necesario disponer de un proceso de obtención, cuantificación e interpretación de datos, al cual se le denomina *medición.* Condiciones importantes para una medición adecuada son:

- Definir claramente qué y con qué se va a medir.
- Definir las escalas y pruebas estadísticas para el análisis de los resultados.
- Describir con detalle el proceso de medición (operacionalización) de las variantes en estudio.
- Especificar las características de la población o de la variable en estudio.
- Unificar los criterios de la medición por parte de los sujetos que la efectuarán.
- Realizar una prueba piloto previa a la medición final para identificar deficiencias y efectuar ajustes.
- Comprobar que el procedimiento de medición sea homogéneo, sobre todo en los sujetos de estudios de casos y controles, para evitar sesgos de mala clasificación.

Resumen

En este artículo se definen los conceptos de ensayo clínico, metaanálisis, sensibilidad y especificidad de una prueba; además, se hace un breve análisis sobre la medicina basada en evidencias. La aplicación de los conceptos epidemiológicos a la neurología y a otras especialidades facilita la interpretación y orientación hacia la aplicabilidad de los resultados de los múltiples estudios que a diario son publicados.

Summary

In this article, we defined the concepts of the clinical trial, meta-analysis, and sensitive had specificity of tests, and included brief information concerning evidence-based medicine. In addition, we described the most recent epidemiologic studies in brief with particular emphasis on those carried out at our setting.

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Aguilar Rebolledo F, Zanabria M.

Late post-acute neurologic rehabilitation: neuroscience, engineering and clinical programs.

Abstract

This lecture highlights my career in rehabilitation research. My principal efforts in rehabilitation have been to study:(1) mechanisms of brain plasticity related to reorganization the brain and recovery of function;(2) late postacute rehabilitation;(3) sensory substitution;(4) rehabilitation engineering. A principal goal has been to aid in the development of a strong scientific base in rehabilitation.

The occasion of the Coulter Lecture is an appropriate time to review the highlights of my career in rehabilitation research. My life-long interest in neuroscience led to a mid-career change, from a professorship in basic science to a resident in physical medicine and rehabilitation. My father had made a dramatic recovery from a major stroke with a home program developed by my brother. After my father's death from a stroke 7 years later while mountain hiking at 9,000 feet (he was still working full-time), the autopsy revealed that recovery had taken place despite very extensive brain damage. The clear demonstration of restarted function by means of rehabilitation was an irresistible stimulus for a career change.

My goal has been to aid in the development of a strong scientific base in rehabilitator Previous areas of research have included brain plasticity and sensory substitution, neuropharmacology, visual cortex and brainstem neurophysiology, and oculomotion.

My principal efforts in rehabilitation have been to study:(1) mechanisms of brain plasticity related to reorganizer of the brain and recovery of function;(2) late post acute rehabilitation;(3) sensory substitution; and(4) rehabilitation engineering.

Key words: Brain, neuronal plasticity, rehabilitation.

Bach-y-Rita, P. Arch Phys. Med. Rehab. 2003: 84:1100-1108.