Valproate Reopens Critical-Period Learning of Absolute Pitch

As children grow they experience critical learning “windows” that allow them to easily absorb new knowledge and develop new abilities, such as how to walk or how to speak. Once the window closes, acquiring the ability becomes difficult or impossible. However, it may now be possible to restore brain plasticity in adults and reopen these critical periods.

Focus of Study

Learning absolute or perfect pitch is a skill that is nearly impossible after about age seven. This study explores whether it is possible to reopen the opportunity for critical-period learning for adults using valproate, a common psychiatric drug.

Background

A critical period is a development stage when children have maximum capacity to acquire abilities ranging from motor skills to language acquisition. During such a period, experience has lasting effects on the development of brain function and behaviour. The principles of critical-period phenomena and neural plasticity are increasingly well understood both at the behavioral and the cellular level. Behaviorally induced brain plasticity, typically at the end of a critical period, can lead to improvement beyond normal performance levels. However, for many tasks, this requires targeted training. At the cellular level, critical periods close when development processes and experiences cause neuro-physiological and molecular changes to remove the potential for further change.

Absolute or “perfect” pitch — the ability to identify or produce the pitch of a sound based only on hearing it — is typically seen in people who started musical training before age six. This indicates a critical period for learning this skill. However, not all children with early musical training develop perfect pitch. If they are not taught to identify pitch classes with labels, they learn relative pitch because it is the basis of language and the Western musical tradition. There are no known cases of adults acquiring perfect pitch.

Histone-deacetylase (HDAC) is an enzyme that acts as an epigenetic “brake” on critical-period learning, leading to decreased plasticity of the brain. Research conducted on adult mice has shown that inhibiting HDAC can allow them to learn habits that are usually impossible to develop after youth.

This is the first evidence that suggests it is possible to reopen the critical period in humans later in life through a drug treatment.
This study assesses whether an HDAC inhibitor, in this case valproate, could reopen plasticity and the opportunity for critical-period learning in adults. Valproate, an anticonvulsant and mood stabilizer, is currently used to treat bipolar disorder and epilepsy.

→ Findings

Valproate significantly improved adults’ perfect pitch performance. Adult men with little or no musical training as children performed significantly better on a test of absolute pitch after two weeks of valproate treatment than after two weeks of placebo. All the men underwent the same ear training during the same period. Those with previous musical training did not perform any better than those with none. In the first treatment arm, the average correct responses were 5.90 in the group who took valproate and 3.50 in the placebo group.

Critical-period learning in humans can be reopened with a drug treatment. The improvement shown in perfect pitch as a result of the valproate treatment suggests that brain plasticity can be at least partly restored later in life. By using a drug to remove the epigenetic brakes on neural plasticity, and reopen the pathways that control critical periods, adults can develop abilities, like perfect pitch, that can typically only be learned in childhood. However, no follow-up testing of the study participants was done to assess how long the improvement in perfect pitch lasted.

CIFAR Program: Child & Brain Development

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→ Methodology

The research team conducted a randomized, double-blind, placebo-controlled study with 24 young men, aged 18-27, who either no or little musical training. Those with training had begun it after aged seven. Blood tests and assessments of mood and cognitive abilities were done before the treatment periods. Perfect pitch was only assessed after treatment because the men did not necessarily already know the names of notes.

In the first treatment arm, the men received either a placebo or valproate for 15 days. On days 8-14, the men completed online ear training exercises that associated six pitch classes from the 12-tone Western musical system.

Musically naïve adults were trained for a short time on several pitch classes, conditions under which no other study has shown any improvement in perfect pitch.
This study is the first to show an improvement in perfect pitch with a drug treatment. The finding that valproate can restore brain plasticity in adulthood in a specific, targeted way provides compelling evidence that its current use in psychiatric treatment may facilitate reorganization and rewiring of otherwise firmly established pathways in the brain and its epigenome. Potential applications include helping recovery in people with a neurodevelopmental disorder, a traumatic brain injury or a stroke.

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