

Study shows correlation between disfunction in neural communication pathways and psychotic disorders

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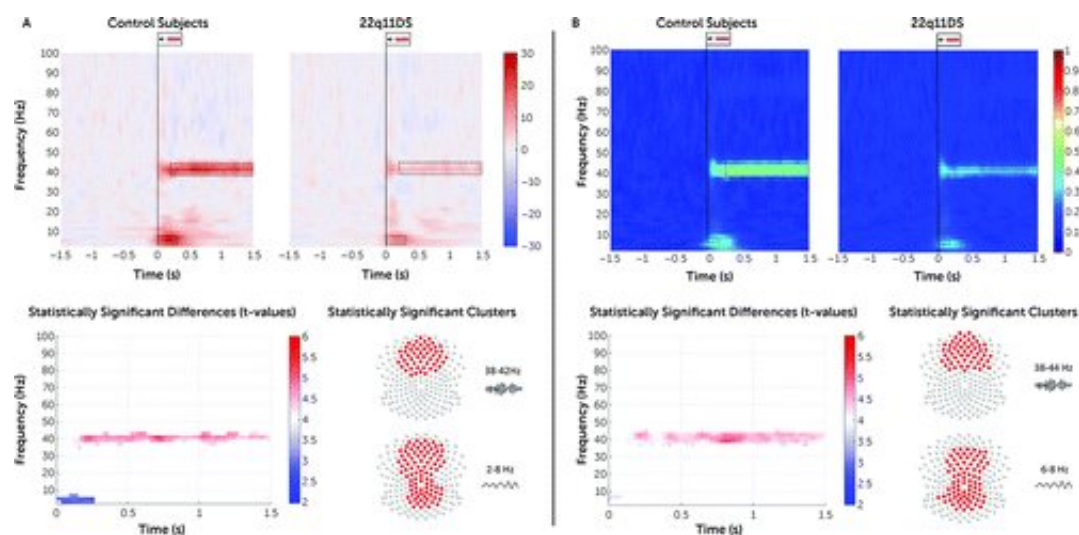


Figure 1. Comparison of ERSP and ITPC between control subjects and 22q11.2 deletion carriers. The top plots in panel A are time-frequency plots displaying the average pre- and poststimulus event-related spectral perturbation (ERSP) in control subjects and deletion carriers, and the top plots in panel B display intertrial phase coherence (ITPC) amplitude in control subjects and deletion carriers. The outlined dotted boxes highlight the time window of statistically significant group differences in gamma and theta power. At the bottom, panel A shows significant delta ERSP and panel B shows significant delta ITPC, with t-values for statistically significant differences in theta and gamma band. Topographical maps display the clusters of electrodes showing statistically significant differences in the gamma and theta bands represented in the time-frequency plots. Power values are expressed in percent. Credit: *American Journal of Psychiatry* (2022). DOI: 10.1176/appi.ajp.2021.21020190

Communication between brain areas is crucial for the brain to correctly process sensory signals and adopt an appropriate behavioral response. Yet, dysfunctions in these communication pathways could be strongly correlated with the onset of schizophrenia. For the first time, a team from the University of Geneva (UNIGE), Switzerland, within the framework of the Synapsy National Centre of Competence in Research, has succeeded in demonstrating this phenomenon in human beings. By carrying out analyses of the brain activity of children, adolescents and young adults with a genetic risk of the disease, the research team has demonstrated that a reduction in the activation of gamma waves, that are known for their role in the proper transmission of information in the brain, was correlated with the emergence of psychotic symptoms even before full-blown disorders appear. This work, published in the *American Journal of Psychiatry*, makes it possible to envisage a very early diagnosis.

In the mammalian brain, the electrical activity of neurons responds to oscillatory rhythms that can be detected by electroencephalography. The coordinated activation of these different waves, which governs, for example, the processing of sensory inputs or the consolidation of memories, enables the brain to function correctly. "We suspected that [gamma waves](#), the highest frequency of the brain rhythms, play a decisive role in the development of schizophrenia symptoms," say Stephan Eliez, professor in the Department of Psychiatry, and Christoph Michel, professor in the Department of Basic Neuroscience, who co-directed the research. "However, we still had to confirm that this impaired synchronization of neural communication pathways observed in mice does indeed exist in humans."

Genetic predisposition

People with a chromosomal microdeletion 22q11 have a 25 to 30% risk of developing schizophrenia in adulthood. "They are therefore a

particularly relevant at-risk population for studying the cerebral development of this disease," says Valentina Mancini, a doctoral student in Stephan Eliez's laboratory and the first author of this study. People with schizophrenia often suffer from reduced capacity to process auditory information; in order to detect any disturbance in brain communication, the scientists therefore measured gamma wave activation following an auditory stimulus in 22q11 patients of all ages, compared with people without this microdeletion.

"Children and adolescents at genetic risk of schizophrenic disorders but without visible symptoms showed the same patterns of gamma wave disruption as patients actually suffering from the disease," explains Vincent Rochas, a scientific collaborator in Christoph Michel's laboratory. In addition, a linear growth of the gamma-band oscillations was observed in people with no [genetic predisposition](#) to schizophrenia, showing a progressive maturation of communication between the cerebral areas during development. "However, this maturation is absent in 22q11 patients, whatever their age, suggesting an abnormal development of circuits underlying neural oscillations in adolescence," stresses Valentina Mancini.

Intervening as early as possible

The research team also identified a strong correlation between the gamma-band activation deficit and the severity of psychotic symptoms, such as auditory hallucinations, thus confirming the existence of a neurobiological progression of the disease. "Our results confirm that this dysfunction appears very early," the authors emphasize. "We now want to identify the best time during the child's development to intervene in relation to this pathological shift."

Moreover, studies on mice show that targeted neuroleptic treatments succeed in correcting neural dysfunctions; in addition, the gamma-band

impairments identified here could be restored using techniques of non-invasive neurostimulation targeting the affected [brain](#) regions, thus opening the way to completely new therapeutic perspectives for treating an often devastating disease.

More information: Valentina Mancini et al, Aberrant Developmental Patterns of Gamma-Band Response and Long-Range Communication Disruption in Youths With 22q11.2 Deletion Syndrome, *American Journal of Psychiatry* (2022). [DOI: 10.1176/appi.ajp.2021.21020190](https://doi.org/10.1176/appi.ajp.2021.21020190)

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