

analysis has the potential to substantially improve treatment efficacy.

Although genotyping for personalized medicine will potentially increase the costs of existing treatment strategies, genotyping costs are dropping rapidly due to advances in technology. More importantly, increased treatment costs can still be cost-effective to the extent that the incremental costs improve patient functioning and increase treatment success rates. For example, use of antidepressant medication increases the cost of treatment in a value-added fashion that justifies the incremental cost, even though antidepressant medication can take weeks to show an effect [10]. Just as pharmacogenetic strategies aspire to match patients to medications to improve efficacy and reduce noncompliance due to side effects, genetically targeted behavioral treatments may also reduce time to remission. Use of a genetic test as a biomarker of a neurocognitive vulnerability (e.g., attention bias) may allow more focused and effective treatments to be provided to those who are most likely to benefit. With an estimated cost of \$700 per day for in-patient treatment for depression, the reduction of hospitalization even by a single day by using a successful genetic matching strategy more than covers the cost of genotyping. The possibility that genetic testing can increase value of treatment efforts more than the cost of the testing itself is an intriguing possibility that has not yet been examined for psychiatric outcomes. This is an important avenue for future research.

In conclusion, we believe that the Eley *et al.* [1] study is an excellent example of why genetic variation can (and should) be incorporated into psychosocial treatment research. This will require close collaboration among experts from diverse fields (e.g., psychologists, geneticists, neuroscientists, statisticians). However, doing so promises to

deliver a fuller, more nuanced understanding of psychopathology which, in turn, could enhance the ability to tailor treatments to individuals based on genetic profile, increase the effectiveness of psychosocial treatments, and ultimately alleviate substantial suffering associated with psychiatric illness.

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### Special Issue: Cognition in Neuropsychiatric Disorders

## Atypical brain oscillations: a biological basis for dyslexia?

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**Examining rhythms in the brain reveals a biological basis for dyslexia. A new study provides evidence of atypical oscillatory patterns and hemispheric specialization in dyslexic adults. These patterns inform phonological processing and verbal memory problems, known to be core deficits in dyslexia.**

A new study published in the December 22 issue of *Neuron* [1] uses an elegant procedure to investigate potential neural mechanisms underlying dyslexia. Dyslexia is a challenging topic and significant controversy has raged

regarding its causes. Nevertheless, amidst the opposing views, there is general agreement that dyslexia is linked to deficits in phonological processes, such as phonological awareness – knowledge of the sounds of language and application of that knowledge to the written word – and phonological memory. Despite this broad agreement, there remains debate about the etiology and nature of the phonological deficit. Precisely what types of speech sounds are troublesome for persons with dyslexia? What form does that difficulty take and what are its underlying neural mechanisms? The article by Katia Lehongre and colleagues [1] addresses these questions using an innovative magnetoencephalographic (MEG) approach and non-speech stimuli.

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Oscillatory brain activity at different frequencies and in different cerebral locations arises when sounds are perceived, stored and manipulated. Capitalizing on the fine spatial and temporal resolution of MEG, Lehongre *et al.* played a slowly-sweeping, frequency-modulated noise stimulus to adults with dyslexia and typical peers. The authors identified cortical regions that oscillated at both 'low gamma', defined here as 25-35 Hz, and higher (45-65 Hz) frequencies. The strength of entrainment to the two oscillation frequencies and their hemispheric distribution differed across the two groups and correlated with task performance on phonological assessments. Many phonetic events occur in a time frame of low gamma, for instance, formant transitions associated with consonants. As a result, the low gamma band (as defined here) is more relevant to speech perception than the 45-65 Hz band. The left hemisphere is particularly tuned to the low-gamma frequency range, whereas processing of slower temporal information (i.e., theta band frequencies, about 4-8 Hz, aligned with the syllable rate of speech) lateralizes to the right hemisphere [2]. Impairment in the processing of both slow and fast temporal components of speech has been suggested to be a key component of developmental dyslexia [3,4]; the Lehongre *et al.* study addresses fast components directly.

In the study, 25-35 Hz oscillatory responses to non-speech sounds are left-hemisphere dominant in controls, consistent with the notion of lateralization of frequencies important to segmental speech. Responses in this frequency range are not left-lateralized in adults with dyslexia, however, who show left-hemisphere dominance in the higher, 45-65 Hz, range instead. Reduced asymmetrical processing of 25-35 Hz and 'oversampling' at sub-phonemic time scales of 45-65 Hz, frequencies beyond the range most useful in phonology, might provide an etiology of dyslexics' deficits in phonological awareness and memory. Specifically, the authors found a negative correlation between 45-65 Hz entrainment and a test of verbal memory. This finding points to a biological basis for the impaired word storage and retrieval in dyslexics – a root impediment underlying phonological processing.

In fact, oversampling might lead to dyslexics placing undue importance on differing speech sounds within a phonemic category. Categorical perception of speech – the grouping together of acoustic tokens that do not cross certain acoustical boundaries – results in sound variations within a category being poorly discriminated by typical readers because they are identified as a single meaningful speech sound instead. In persons with dyslexia, discrimination of within-category acoustic contrasts is actually superior to controls, possibly leading to confusion in phoneme-to-grapheme mapping [5]. Findings from another study [6] parallel this idea of abnormal categorical speech processing in dyslexics: this study showed, via speech-evoked auditory brainstem responses, that children with dyslexia are less able to profit from speech sound regularity than normal readers but instead exhibit excessive sensitivity to variably-presented speech. Subsequent work has broadened this finding to rhythm-processing in a non-linguistic (musical) context, suggesting that reading draws on temporal pattern detection mechanisms common to speech and music [7].

Lehongre *et al.*'s intriguing findings support a temporal sampling framework for reading [3] and open the door to future investigations of this nature. An obvious extension of this approach would be to examine theta-band oscillations in persons with dyslexia. This band encompasses the time scale of prosody, which has been shown to be right-hemisphere lateralized. Processing deficits in this frequency range have been found in persons with dyslexia [8,9], suggesting that sampling deficits might be found across the brain oscillatory ranges important for speech perception.

A second line of follow up research could investigate evoked oscillatory activity in children. Although the MEG measure employed was elicited passively, it is almost certain that a person's prior active engagement with sound contributes to the observed effect. The auditory system is massively influenced by experience and development [10]; every structure, from the cortex to the cochlea, is enervated by efferent connections that exert 'top-down' influence. The 'normal' pattern of gamma oscillations seen in the control group likely is not strictly hard-wired, but also represents years of language experience. Similarly, the abnormal gamma activity seen in dyslexic adults may stem from their lifelong impairments with phonological processing. The immature auditory system – both normal and dyslexic – may show different patterns of oscillatory activity.

In sum, by examining rhythms in the brain, the results of Lehongre and colleagues demonstrate neural correlates of phonological processing and verbal memory problems known to be core deficits in dyslexia and provide a viable approach for future investigations.

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