Comparing Clinical Efficacy of C5, C3 and Factor B Inhibition in Paroxysmal Nocturnal Hemoglobinuria

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Abstract

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, life-threatening hematologic disorder that is caused by unregulated complement activation, leading to chronic red blood cell (RBC) hemolysis, anemia, fatigue, and an increased risk of thrombosis. The therapeutic landscape for PNH includes three key complement-targeting agents: ravulizumab (C5 inhibitor), pegcetacoplan (C3 inhibitor), and iptacopan (factor B inhibitor), each acting at different points in the complement cascade and demonstrating variable clinical efficacy. This study evaluates each treatment's clinical effectiveness through a comparative analysis of six pivotal phase III trials, integrating primary and key secondary endpoints as well as commonly reported PNH biomarkers. The analysis encompasses both treatment-naïve patients and those transitioning between complement inhibitors. Findings suggest that factor B inhibition provides the most robust overall clinical efficacy, while C3 inhibition offers superior protection against hemolysis by blocking complement activation at an earlier stage. Although C5 inhibition remains a viable treatment option, it is associated with a higher likelihood of breakthrough hemolysis. However, limitations of this comparison of pivotal phase III trials include: heterogeneity in patient baseline characteristics, differences in trial design, variability in endpoint selection, and discrepancies in biomarker reporting. Ultimately, this work demonstrates the need for a greater understanding of the complement cascade and the effects of its inhibition at different points of activation in relation to diseases, such as PNH, that arise from its dysregulation.

Sexual and Gender Minority Youth in ACCESS Open Minds: Severity at Presentation to Diverse Youth Mental Health Services

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Abstract

Childhood and adolescence are crucial periods in the development of healthy individuals. They are periods of significantly increased vulnerability to developing mental illness. Among youth, sexual and gender minorities face greater adversity and higher mental health risks than their cisgender and heterosexual peers, with gender minorities experiencing worse outcomes than sexual minorities. While substantial research has examined adversities and mental health disparities for sexual and gender minority youth relative to the general population, no study has investigated how severity at presentation to healthcare services differs between sexual and gender minorities. Since gender minorities face more adversity, it was hypothesized that their severity at the initial assessment would be higher. Using the ACCESS Open Minds database, which includes data from 5,232 youth aged 11 to 25 who were referred for or sought mental health help at 12 diverse sites across Canada, the severity of mental health presentations of 722 sexual minority youth and 258 gender minority youth was analyzed. Severity was determined by scores on the Kessler Psychological Distress Scale (K10), Clinical Global Impression (CGI) scale, and the Social and Occupational Functioning Assessment Scale (SOFAS). No significant differences were found for K10 and CGI, but gender minority youth had significantly lower SOFAS scores than sexual minority youth. Differences in social and occupational functioning without differences in severity of mental distress may reflect an important role for social discrimination against gender minorities and its consequent impact on the social and vocational possibilities for these youth.

It's Not Always Black and White: How Color Enhances L1 and L2 Idiom Processing

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Abstract

Idioms are non-compositional expressions whose meanings transcend the literal interpretation of their components (e.g., "break the ice"). They highlight the psycholinguistic tension between direct retrieval and compositional semantic analysis. Past research suggests L1 readers rely more on direct retrieval and idiom familiarity, while L2 readers depend more on word-by-word compositional processing. Supporting this, studies show that disrupting an idiom's canonical form impacts L1 readers more than L2 readers. This study explored the reverse effect by strengthening an idiom's canonical form through font color. L1 and L2 readers read English sentences containing idiomatic/literal phrases, presented in colored/standard font, and judged whether the phrases made sense. Accuracy and reaction times were recorded. In L1 readers, idiom superiority (i.e., better performance for idioms than literal phrases) was driven by familiarity, with color coding enhancing this effect for more familiar idioms. In L2 readers, idiom superiority was influenced by both familiarity and decomposability, with color coding amplifying both effects. These findings suggest that L1 readers primarily rely on direct retrieval, whereas L2 readers utilize both direct retrieval and compositional processing, with color coding aiding idiomatic processing for both groups.