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Fragile X International (Fraxi.org)

Press Release

Fragile X International (FraXI) thanks everyone for the widespread use of the term Fragile X Premutation Associated Conditions (FXPAC) to describe issues affecting fragile x premutation carriers (see Notes).

Just as Fragile X Syndrome is an umbrella term which covers the many issues that may affect someone with more than 200 CCG repeats of the FMR1 gene, so FXPAC is a general term which covers all the issues that someone with between 50-200 CGG repeats of the FMR1 gene may experience.

In 2020, two of FraXI's board members and one of their specialist advisors co-authored an article in a leading academic journal, *Frontiers*, entitled **Fragile X Premutation Associated Conditions**, which you can read [here](#). In that article, they called for removal of the word 'disorder' from fragile x associated premutation terminology.

FXPAC is an inclusive term, introduced because of the stigmatisation many carriers have experienced at work, in their private lives and in wider society. Specifically, the proposal of the new term FXAND (FX-associated neuropsychiatric disorders) in 2018 caused dismay amongst FX premutation carriers because of the use of the word 'disorder' to refer to issues which may affect them.

FXPAC encompasses the longer list of issues researchers have now shown affect fragile x premutation carriers. FXPAC was developed in conversation with 17 family-led fragile x country organisations, following a workshop at the European Fragile X Network conference in Rotterdam in 2019. Since then, further country organisations have expressed support, with the majority of family-led fragile x organisations worldwide endorsing the term FXPAC.

It is vital to listen to the families and carriers, those whose daily lives and identities are affected by these terms. Fragile X Premutation Associated Conditions is a term which lists everything which may or may not affect a premutation carrier, it is non-offensive and non-discriminatory. We welcome the research many are doing in this field, and welcome the fact that researchers going forward are using this inclusive terminology.

In the years since publication in 2020, it has become more clear that FXPAC is a unifying, overarching term. Now, with the number of potential fx premutation carrier issues growing

longer, it may be that a list such as the following could be used (with the individual items requiring further research leading to stronger evidence):

Fragile X Premutation Associated Conditions

- Fibromyalgia, muscle pain, chronic pain
- Migraines
- Sleep apnea
- Hyperthyroidism
- Chronic fatigue syndrome
- Cardiovascular problems
- Osteoporosis
- Anxiety
- Depression
- Primary Ovarian Insufficiency (FXPOI)
- Tremor/Ataxia (FXTAS or FX-associated Tremor/Ataxia Syndrome)

However, if researchers prefer further definition, then the extra terms included in the *Frontiers* (Johnson et al, 2020) article would be sufficient: Fragile X-associated Neuropsychiatric Conditions (FXANC) and Fragile X Various Associated Conditions (FXVAC).

We are grateful for all of the research being conducted in this field, and for the support of researchers in using terminology which is positive, affirming and inclusive.

Notes:

Frontiers article: [Frontiers | Fragile X Premutation Associated Conditions \(FXPAC\) \(frontiersin.org\)](https://www.frontiersin.org/articles/10.3389/fpsyg.2020.00101/full)

FXPAC has now been cited in 25 scientific articles and books, including:

“Over the past two decades, while the general population exhibit in average 30 CGG repeats, premutations between 50 and 200 repeats in the FMR1 gene have been associated with Fragile X Premutation Associated Conditions (FXPAC), a set of conditions with no intellectual disability. Also, it is important to note that mutations in the FMR1 gene are incompletely penetrant, and some individuals, in particular females bearing abnormal CGG repeat expansions will exhibit no signs of FXS or FXPAC.”^[1]

“Individuals with the premutation do not express the severe phenotypes seen with the full mutation however several disorders are associated with premutation carriers, namely, fragile X-associated tremor and ataxia syndrome (FXTAS), fragile X associated primary ovarian insufficiency (FXPOI), and fragile X premutation associated conditions (FXPAC).”^[2]

“These results strongly support the need for recognition of a behavioural and cognitive phenotype for women with the FX-p and support the newly proposed term of fragile-X-associated neuropsychiatric conditions. Early recognition and identification of these challenges will be important for providing appropriate levels of support for women with the FX-p and their families.”^[3]

“Since the FMR1 gene was identified in 1991, the premutation-related clinical conditions have been reported. Various health conditions have been found in carriers, named “fragile X premutation associated conditions (FXPAC).^[4] FXPAC includes fragile X-associated tremor/ataxia syndrome (FXTAS), fragile X-associated primary ovarian insufficiency (FXPOI), fragile X-associated neuropsychiatric disorder (FXAND).”^[5]

“Women with a PM are also at risk for Fragile X Premutation Associated Conditions (FXPAC) which include fragile X-associated primary ovarian insufficiency (FXPOI), fragile X-associated tremor-ataxia syndrome (FXTAS), and Fragile X-Associated Neuropsychiatric Disorders (FXAND).”^[6]

[1] [Frontiers | FMRP, a multifunctional RNA-binding protein in quest of a new identity \(frontiersin.org\)](#)

[2] [Genes | Free Full-Text | FMR1 and Autism, an Intriguing Connection Revisited \(mdpi.com\)](#)

[3] [Autistic traits and mental health in women with the fragile-X premutation: maternal status versus genetic risk | The British Journal of Psychiatry | Cambridge Core](#)

[4] [Frontiers | Fragile X Premutation Associated Conditions \(FXPAC\) \(frontiersin.org\)](#)

[5] [Fragile X premutation and associated health conditions: A review - Tassanakijpanich - 2021 - Clinical Genetics - Wiley Online Library](#)

[6] [Frontiers | Predictors of Comorbid Conditions in Women Who Carry an FMR1 Premutation \(frontiersin.org\)](#)

For more information, press only:

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