

Fragile X Mental Retardation Protein and cerebral expression of metabotropic glutamate receptor subtype 5 in men with fragile X syndrome: a pilot study

Legends

Table S1. Concomitant medications of participants with from the Institute for Neurodegenerative Disorders (IND)

Medication: 0 = absent, 1 = present

FXS: Fragile X syndrome

FXS-M: Fragile X syndrome mosaicism

. (period) = Missing data

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Table S2. Demographic and clinical characteristics of participants from the Institute for Neurodegenerative Disorders (IND)

All participant are non-Hispanic.

AA: African American

Age: Age in years

BMI: Basal metabolic index

C: Caucasian

FXS: Fragile X syndrome

FXS-M: Fragile X syndrome mosaicism

Ht: Height in inches

ID: Identification

TD: Typical development

Wt: Weight in pounds

. (period) = Missing data

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Table S3. Demographic and clinical characteristics of participants from the Johns Hopkins University (JHU)

A: Asian

AA: African American

Age: Age in years

BMI: Basal metabolic index

C: Caucasian

FXS = Fragile X syndrome

Hispanic: 0 = not Hispanic, 1 = Hispanic

Ht: Height in inches

ID: Identification

IASD: Idiopathic autism spectrum disorder

Male: 0 = female, 1 = male

Race: A = Asian, AA = African American, C = Caucasian

TD: Typical development

Wt: Weight in pounds

. (period): Missing data

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Table S4. Genetic and psychological assessments of participants from the Institute for Neurodegenerative Disorders (IND)

AGG: Adenosine guanine guanine

CGG: Cytosine guanine guanine

DNA: Deoxyribonucleic acid

DSQIID; Dementia Screening Questionnaire for Individuals with Intellectual Disabilities (Deb S et al., 2007)

FMRP: Fragile X Mental Retardation Protein in nanograms per microgram total protein

FXS: Fragile X syndrome

FXS-M: Fragile X syndrome mosaicism

ID: Identification

kb: Kilobase

MMSE: Mini-Mental State Examination (Folstein MF et al., 1975)

ng: Nanogram

TD: Typical development

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Table S5. Genetic and psychological assessments of participants the Johns Hopkins University (JHU)

%-ile: Percentile

ADOS-2: Autism Diagnostic Observation Schedule, 2nd Edition (Lord C et al., 2012)

CANTAB IED: Cambridge Neuropsychological Test Automated Battery Intra/Extra Dimensional Set Shift (Cambridge Cognition Ltd., 2020)

CANTAB OTS = Cambridge Neuropsychological Test Automated Battery One Touch Stockings of Cambridge (Cambridge Cognition Ltd., 2020)

DNA: Deoxyribonucleic acid

FMR1: Fragile X Mental Retardation 1

FMRP: Fragile X Mental Retardation Protein

FXS: Fragile X syndrome

FXS-M: Fragile X syndrome mosaicism

HVLT: Hopkins Verbal Learning Test–Revised™ (Benedict RHB et al., 1998; Brandt J et al., 1998; Shapiro AM et al., 1999)

ID: Identification

IQ: Intelligence quotient

mRNA: Messenger ribonucleic acid

RRB: Restricted and repetitive behaviors

SA: Social affect

SB-5: Stanford-Binet Intelligence Scales, Fifth Edition (Roid GH, 2003)

TD: Typical development

TDPM: Typical development premutation

Vineland-3: Vineland Adaptive Behavior Scales, Third Edition (Sparrow SS et al., 2020)

. (period) = Missing data

## Fragile X Mental Retardation Protein and cerebral expression of metabotropic glutamate receptor subtype 5 in men with fragile X syndrome: a pilot study

Table S6. Fragile X Mental Retardation Protein (FMRP) in nanograms per microgram total protein for ten healthy people with typical development (TD) with normal CGG repeat sizes [range (20, 37)] utilizing the same analyses as other participants

CGG: Cytosine guanine guanine

Table S7. Positron emission tomography (PET) data and analyses for participants from the Institute for Neurodegenerative Disorders (IND)

Statistical Parametric Mapping (SPM) (Wellcome Centre for Human Neuroimaging, 2020) was applied to PET frames to obtain regional time activity (radioactivity) curves (TACs) on an ECAT EXACT HR+ PET (Wienhard K et al., 1994) after an intravenous bolus injection of 185 MBq (5 mCi) [<sup>18</sup>F]FPEB (Wong DF et al. 2013) for participants with FXS and TD. Ratios of uptake in the regions of interest (ROIs) to the uptake in the cerebellum, a reference region with minimal [<sup>18</sup>F]FPEB uptake (Sullivan J et al., 2012; Sullivan JM et al., 2013), were calculated (Brašić JR et al., 2020, 2021).

INDTD30 underwent a second testing identified as 2INDTD30.

[<sup>18</sup>F]FPEB: 3-[<sup>18</sup>F]fluoro-5-(2-pyridinylethynyl)benzotrile

FXS: Fragile X syndrome

FXS-M: Fragile X syndrome mosaicism

mCi: Millicurie

MBq: Megabequerel

PET: Positron emission tomography

ROI: Region of interest

TD: Typical development

. (period) = Missing data

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Table S8. Positron emission tomography (PET) data and analysis of participants from the Johns Hopkins University (JHU)

Nondisplaceable binding potentials ( $BP_{ND}$ ) (Innis RB et al., 2007) for both the reference tissue graphical analysis (RTGA) (Logan J et al., 1996, 2011) and the multilinear reference tissue method with two parameters (MRTM2) (Ichise M et al., 2002) for cerebral regions of interest by positron emission tomography (PET) for 90 min after intravenous bolus injections of 185 megabecquerels (MBq) [5 mCi] [ $^{18}F$ ]FPEB (Wong DF et al., 2013) to participants with FXS and IASD and ID (N = 2), IASD (N=7) (Fatemi SH et al., 2018), and typical development (TD) (N=7) (Fatemi SH et al., 2018).  $BP_{ND}$ s for participants with TD and IASD were performed at different times with different analytical techniques. Therefore, there are inconsistencies in the procedures used to generate the results for TD and IASD (Brašić JR et al., 2020, 2021).

[ $^{18}F$ ]FPEB: 3-[ $^{18}F$ ]fluoro-5-(2-pyridinylethynyl)benzonitrile (Wong DF et al., 2013)

Am: Amygdala

aFr: Anterior frontal cortex

aTp: Anterior temporal cortex

$BP_{ND}$ : Nondisplaceable binding potential (Innis RB et al., 2007)

cAC: Caudal anterior cingulate

Cb: Cerebellum

Cg: Cingulate

CN: Caudate nucleus

Cu: Cuneus

dpTp: Dorsal posterior temporal cortex

ER: Entorhinal area

FO: Frontal operculum

Fr: Frontal cortex

Fs: Fusiform gurus

FXS: Fragile X syndrome

GP: Globus pallidus

Hp: Hippocampus

IASD: Idiopathic autism spectrum disorder

## Fragile X Mental Retardation Protein and cerebral expression of metabotropic glutamate receptor subtype 5 in men with fragile X syndrome: a pilot study

IC: Isthmus/cingulate

ID: Intellectual disability

In: Insula

iPa: Inferior parietal cortex

iTp : Inferior temporal cortex

IOc: Lateral occipital cortex

I OG: Lateral orbital gyrus

LG: Lingual gyrus

MBq: Megabecquerel

mCi: Millicurie

mdOG: Medial orbital gyrus

mFr: Middle frontal cortex

MRTM2: Multilinear reference tissue method with two parameters (Ichise M et al., 2002)

mTp: Middle temporal cortex

Oc: Occipital cortex

OO: Orbital operculum

Pa: Parietal cortex

paC: Paracentral

pC: Pericalcarine cortex

pCg: Posterior cingulate

PET: Positron emission tomography

PH: Parahippocampus

Pr: Precuneus

Prc: Precentral gyrus

PS: Postcentral gyrus

PT: Pars triangularis

Pu: Putamen

rAC: Rostral anterior cingulate

# Fragile X Mental Retardation Protein and cerebral expression of metabotropic glutamate receptor subtype 5 in men with fragile X syndrome: a pilot study

rFr: Rostral frontal cortex

ROI: Region of interest

RTGA: Reference tissue graphical analysis (Logan J et al., 1996, 2011)

sFr: Superior frontal cortex

SM: Supramarginal

sPa: Superior parietal cortex

sTp: Superior temporal cortex

TD: Typical development

Th: Thalamus

Tp: Temporal lobe

tT: Transverse temporal

vS: Ventral striatum

. (period) = Missing data

Table S9. Correlation coefficients between Fragile X Mental Retardation Protein (FMRP) (Table S4) and [18F]FPEB uptake (Wong DF et al. 2013) for participants with fragile X syndrome (Table S7).

Row 9 Correlation coefficient with FMRP (Microsoft (R) Excel for Mac Version 16.56 2021)

Row 11 Pearson R with FMRP (Stangroom 2021)

Row 12 Probability of Pearson R with FMRP (Stangroom 2021)

[18F]FPEB: 3-[18F]fluoro-5-(2-pyridinylethynyl)benzotrile

FMRP: Fragile X Mental Retardation Protein in nanograms per microgram total protein

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Table S10. Correlation coefficients between Fragile X Mental Retardation Protein (FMRP) (Table S4) and [18F]FPEB uptake (Wong DF et al. 2013) for participants with fragile X syndrome and fragile X syndrome-mosaicism (Table S7).

Row 9 Correlation coefficient with FMRP (Microsoft (R) Excel for Mac Version 16.56 2021)

Row 11 Pearson R with FMRP (Stangroom 2021)

Row 12 Probability of Pearson R with FMRP (Stangroom 2021)

[18F]FPEB: 3-[18F]fluoro-5-(2-pyridinylethynyl)benzonitrile

FMRP: Fragile X Mental Retardation Protein in nanograms per microgram total protein

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