BRO E ALTERAÇÃO EM TESTE DE COGNIÇÃO PRÉ-FRONTAL

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Introdução: O fator neurotrófico derivado do cérebro (BDNF) é uma neurotrofina e tem se mostrado um potente modulador da transmissão sináptica e plasticidade no sistema nervoso central, participando dos processos cognitivos como o aprendizado e a memória. Recentemente, o gene do BDNF tem se mostrado um gene candidato para estudo da patogenia em doenças psiquiátricas. Atualmente, dois polimorfismos deste gene já foram identificados: o polimorfismo de dinucleotídeos em repetição e o polimorfismo de um único nucleotídeo Val66Met. Recentes estudos demonstram uma associação entre ambos os tipos de polimorfismos e o transtorno bipolar. Déficit de desempenho cognitivo no pré-frontal têm se mostrado como um possível marcador na doença bipolar. Objetivos: O presente estudo teve por objetivo avaliar a associação do polimorfismo do gene do fator neurotrófico derivado do cérebro (BDNF) e a performance cognitiva através do Teste Wisconsin de Classificação de Cartas (WCST) em pacientes bipolares Materiais e métodos: Foram avaliados 58 pacientes, 14 do gênero masculino e 44 do gênero feminino, sendo a idade média 40 anos (de18 a 68 anos de idade). Foi analisada a associação entre a presença do alelo Met do polimorfismo (val66met) do BDNF e o número de erros perseverativos (WCST-P), número de erros não perseverativos (WCST-NP), resposta de nível conceitual (WCST-%CONC), número de categorias completadas (WCST-CC) e ensaios para completar a primeira categoria (WCST- 1st CAT). Resultados e conclusões: O percentual de indivíduos Val/Val, Val/Met e Met/Met foi respectivamente 48,4%, 24,2% e 4,8%. Não houve diferença entre os grupos portadores e não portadores do alelo Met em relação a sexo, idade, início da doença, números de anos estudados nem tempo de evolução da doença. O desempenho do grupo de portadores do alelo Met (Val/Met e Met/Met) apresentou um pior desempenho no domínio de erros não perseverativos (p

PANIC DISORDER AND SEROTONINERGIC GENES (5-HTTLPR, HTR1A AND HTR2A): ASSOCIATION AND INTERACTION WITH CHILDHOOD TRAUMA AND PARENTING.

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**Background**: Panic disorder (PD) has been related genetic and environmental risk factors. However, no study has evaluated a gene-environment interaction for this disorder. The aim of this study is to evaluate the association between HTR1A, HTR2A and 5-HTTLPR and PD. We also ought to evaluate the interaction between these genes and two environmental factors previously associated with PD: childhood trauma and parental bonding. **Methods**: This is a case-control candidate gene study (107 PD patients and 125 controls). Diagnoses were confirmed by M.I.N.I and clinical interview. Childhood trauma was evaluated by the Childhood Trauma Questionnaire (CTQ) and Parental Bonding Instrument (PBI) was used to evaluate parenting. Genes were screened using a set-based test in PLINK software followed by single marker association tests and haplotype test for genes that reached experiment-wide significance. Logistic regression was used to model gene-environment interaction. We addressed multiple comparisons at two levels of significance correction: gene-wide ($p_1$) and experiment-wide ($p_2$). **Results**: Only HTR1A was experiment-wide associated with PD in set-based test ($p_2$=0.027). Regarding interaction analysis with optimal father parenting, interaction terms HTR2A SNPs (rs6311 and rs6313) were nominally associated with PD and rs6311 remained significant at gene-wide level of correction. Among subjects with TT/TC genotype in rs6311 the protection effect of fathers with high care and low overprotection was higher than the protection effect among subjects with CC genotype ($\beta$=0.134, t=-2.678, $p_0$=0.007, $p_1$= 0.042). **Conclusion**: We replicated association between the HTR1A promoter SNP (rs6295) and PD, but did not observe association with HTR2A or 5-HTTLPR. We also reinforce evidence of gene-environment interaction in HTR2A gene with parenting, maybe influencing the capacity of subjects to use familiar experiences as environmental support.

VARIANTS IN A GENE ENCONDING A REGULATOR OF G PROTEIN SIGNALING 4 (RGS4) ARE ASSOCIATED WITH THE COMORBIDITY BETWEEN PANIC DISORDER (PD) AND SOCIAL ANXIETY DISORDER IN PD PATIENTS

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**Background**: Recent evidences suggest that the genes encoding regulators of G proteins (RG) as RGS2 (RG signaling 2) and RGS4 (RG signaling 4) are implicated in childhood temperament as behavioral inhibition, an intermediate phenotype tightly related with Social Anxiety Disorder in adulthood. The aim of this study was to examine whether variants in RGS2 and RGS4 genes are associated with the comorbidity between Panic Disorder (PD) and Social Anxiety Disorder (SAD) in PD patients. **Methods**: This is a candidate-gene association study with 127 PD patients diagnosed by M.I.N.I. (106 without comorbidity with SAD and 21 with comorbidity with SAD). We have examined 22

single nucleotide polymorphisms (SNPs) 15 of RGS2 and 7 of RGS4. Genes were screened using a set-based test (a multiallelic test) in PLINK software followed by single marker association tests, using permutation procedure in order to control for multiple comparison. **Results**: In the set-based test only RGS4 achieve experiment-wide significant association with the comorbidity with SAD (p=0.046). Out of the 7 RGS4 single markers SNPs, two (rs12402634 and rs10917672) showed nominally (OR =0.22; CI95% 0.07 to 0.63; p=0.002) and empirically significant associations that survival correction for the 22 SNPs included in the analysis (corrected p-value 0.040). These two SNPs are in perfect Linkage Disequilibrium. **Conclusion**: In sum, we observed evidence of association between a variant in RGS4 and comorbidity with SAD in PD patients. RGS4 was previously implicated in antihypertrophic effect of secreted natriuretic peptides in the heart and maybe this association with SAD could explain why phobic patients are at higher cardiovascular risk with impact in mortality rates. This study intend to generate hypothesis for future larger studies, designed to confirm this association *a priori* in order to better understand the relation between these variables. Additionally, replication is needed.

## AGE OF FIRST ALCOHOL USE AND OPINION ABOUT DUI ENFORCEMENT ARE ASSOCIATED WITH DRINKING AND DRIVING IN BRAZILIAN DRIVERS

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Brazil lacks information about driving under the influence of alcohol (DUI), particularly with data from representative samples from the general population. Anecdotal information suggests a high prevalence of DUI among young Brazilian males. Method: 333 subjects with driver licenses and who drank in the last 12 months were drawn from a random sample of 2,346 adults (18 to 79 years old) from the first Brazilian household survey of patterns of alcohol use. Bivariate analysis tested the association between demographics, type, frequency, and quantity of alcohol used; binge drinking; drinking places; passenger of a drunk driver; frequency of drunk driving accidents; age of first drink; alcohol abuse; alcohol dependence; perceptions about drunk driving and “having driven after drinking at least three units of alcohol”.Data were then submitted to multivariable regression analysis. Results: Being male, an alcohol abuser/dependent ,and having started to drink between 16 and 17 remained independently associated with heavy drinking and driving after model adjustments. The same is true for having been a passenger in a vehicle where the driver was drinking, as well as a previous DUI accident.. Higher support for DUI enforcement was protective against drinking and driving. Comments: Risk factors for DD in a representative sample of Brazilian adults are similar to those reported in other countries, except for the perception of punishment. Interestingly, it seems that even having strong opinions about DUI enforcement, those subjects do not perceive punishment as effective in the country, which might contribute to the elevated levels of risk factors associated with DD in this sample.

## SUPERPROTEÇÃO MATERNA MODIFICA OS EFEITOS DE MAUS TRATOS NA INFÂNCIA NO TRANSTORNO DO PÂNICO EM MULHERES: UM ESTUDO DE INTERAÇÃO

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Objetivo: Avaliar a interação entre a história de trauma na infância e o tipo de parentagem em pacientes adultos do sexo feminino com transtorno do pânico (TP). Método: 87 mulheres com TP e 87 controles femininos pareados por idade e renda foram avaliadas por uma entrevista clínica e MINI (Mini Internacional Neuropsychiatry Interview). Trauma na infância foi avaliado através da aplicação do questionário CTQ (Childhood Trauma Questionnaire) e o tipo de parentagem foi avaliado usando-se o instrumento PBI (Parental Bonding Instrument). Resultados: Trauma na infância (OR=2,30; p=0,043) e superproteção materna (OR=2,32; p=0,009) foram associados a uma maior chance de TP na vida adulta em mulheres. A interação entre a mãe superprotetora e a lembrança do trauma teve associação estatisticamente significativa com TP (p=0,025). Entre as mulheres sem a superproteção maternal, o OR entre trauma e TP foi de 4,40 (95%IC 1,50 à 12,90; p=0,006). Por outro lado, entre as mulheres com mãe superprotetora, o OR entre trauma e TP foi de 0,57 (95%IC 0,14 à 2,36; p=0,518). Conclusão: Em nosso estudo, a superproteção materna pôde funcionar como um efeito tamponante em relação à situação traumática, ajudando na superação de eventos estressantes e evitando TP na vida adulta em mulheres. Mais estudos são necessários para confirmar essa hipótese.

## TRANSTORNOS DEPRESSIVOS: UM NOVO MODELO PARA DEFINIR MELANCOLIA

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O DSM-IV-TR trata melancolia como um especificador do Episódio Depressivo Maior, considerando aspectos como humor não reativo, anedonia, insônia terminal, culpa, alterações psicomotoras e de apetite/peso. Segundo alguns autores, a população identificada como melancólica pelo DSM forma um grupo de