Associations between genetic variations and global motion perception

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Abstract

The cholinergic system is known to strongly modulate perceptual and cognitive processes, and the alpha7 subunit of the cholinergic nicotinic receptor (CHRNA7) is broadly expressed within the visual system. Here, we assessed whether genetic variations of the alpha7 subunit of the cholinergic nicotinic receptor gene (CHRNA7) affect coherent motion perception. Motion perception has been shown to decline with age, and it has previously been suggested that effects of genetic variations are magnified by age. Therefore, we tested both older (n=62) and younger adults (n=63). We found that motion coherence thresholds were significantly higher for older compared to younger adults, in accordance with previous studies. Interestingly, there was a strong relationship between variants of the SNP rs2337980 of the CHRNA7 and motion direction discrimination. In particular, participants carrying the TC genotype had considerably lower motion coherence thresholds than CC carriers. The effect of genotype did not interact with age. Our results show that genetic variations are associated with perceptual performance but are unlikely to explain age-related changes.

Keywords Coherent motion, Genetic variations, Cholinergic system, CHRNA7, Aging

Introduction

Visual perception is strongly influenced by the neuromodulator acetylcholine. For example, studies in macaque monkeys have demonstrated that the cholinergic system up- and down regulates the incoming visual information in the primary visual cortex (Disney et al. 2007) and enhances visual perception (Kang et al. 2014). Increasing acetylcholine by the cholinesterase inhibitor donepezil improves perceptual learning in humans (Rokem & Silver 2010). In addition, visual backward masking is impaired after nicotine deprivation in chronic smokers, suggesting a strong link between nicotine levels and visual temporal processing (De Leon & Diaz 2005; Leonard et al. 2007; Kunchulia, Pilz & Herzog 2014). The alpha7 subunit of the cholinergic nicotinic receptor gene (CHRNA7) is of particular importance with regards to perception, because it is broadly expressed in the visual system including the retina and the primary visual cortex (V1; Aztiria et al. 2004; Gotti et al. 2007; Galvin et al., 2018), and visual acuity is reduced in alpha 7 nicotinic receptor knockout mice (Origlia et al. 2012). Genetic alternations of α7-nAChR have been reported in a variety of disorders such as schizophrenia (Severance & Yolken, 2008), autism spectrum disorder (Deutsch et al., 2011) and Alzheimer's disease (Parri, Hernandez, Dineley et al., 2011). These disorders are all accompanied by substantial deficits in visual perception (Chen, Nakayama, Levy, Matthysse, & Holzman, 2003; Spencer, Sekuler, Bennett, & Christensen, 2013; Koldewyn, Whitney, & Rivera, 2010; Robertson et al., 2014; Fernandez, Monacelli & Duffy, 2013). Given the broad expression of the α7-nAChR in the visual system, it is reasonable to assume a relationship between these genetic alterations and deficits in visual perception. Despite CHRNA7 being an attractive candidate for investigating the relationship between common genetic variations and visual perception, its relationship with visual perception in humans has rarely been studied. However, Bakanidze and colleagues (2013) found that a single nucleotide polymorphism (SNP) of the CHRNA7 correlates with visual backward masking deficits in schizophrenic patients. Up to

date, no studies have investigated possible correlations between genetic variations of the alpha7 subunit of the cholinergic nicotinic receptor gene and visual perception in the healthy population, a link that would emphasize its importance in visual perceptual functions in mental disorders and potentially help to intervene at an early stage of the disease.

Here, we tested whether SNPs of the CHRNA7 play a role in motion perception in neurotypical healthy adults. Motion perception is a fundamental part of visual perception that allows us to discriminate the movement of objects in the world around us (Hutchinson, Ledgeway, Allen, 2014). Motion perception starts in retinal ganglion cells that project to the lateral geniculate nucleus (LNG), in particular the magnocellular system for motion perception (Maunsell, Nearly and DePriest, 1990, see also Billino & Pilz 2019). The LGN projects further to neurons in the primary visual area (V1). Global motion is processed in the middle temporal area (hMT/V5), which receives direct connections from V1 and indirect ones via V2 and V3 (McCool & Britten, 2008). We included younger and older participants in our study, because it has been suggested that effects of common genetic variations on cognitive functions are magnified by age, thus, increasing inter-individual differences (Papenberg, Lindenberger & Backman 2015; Papenberg et al. 2015). In addition, visual motion perception is the most studied perceptual ability in healthy ageing and therefore, can be used as a conceptual model for studying perceptual aging (see Billino & Pilz 2019, for a review). It has been shown that older adults are worse than younger adults at detecting, discriminating, and identifying the direction of global motion in random-dot kinematograms (Ball & Sekuler 1986; Bennett, Sekuler & Sekuler 2007; Billino, Bremmer, & Gegenfurtner 2008; Hutchinson et al. 2012; Hutchinson et al. 2014; Tran, Silverman, Zimmerman & Feldon 1998; Trick & Silverman 1991). However, large individual differences in performance exist within the group of older adults in that some older participants perform on the level of younger adults, whereas others show large deficits in performance (e.g., Billino et al. 2009; Norman et al. 2013; Pilz et al.

2015; Shaqiri et al. 2015, Pilz et al. 2017; Shain and Norman 2018). The magnitude of the age-related deficit strongly depends on stimulus parameters such as speed (Snowden & Kavanagh 2006), motion coherence (Pilz, Miller & Agnew 2017), motion direction (Pilz et al. 2017; Shain and Norman 2018) and contrast (Allen, Hutchinson, Ledgeway & Gayle 2010), factors that affect performance on an individual level. These individual differences suggest that age alone cannot explain age-related deficits in motion perception. Given that cognitive effects of common genetic variations are magnified by age (Papenberg, Lindenberger & Backman 2015; Papenberg et al. 2015), individual differences in motion perception could also be related to genetic variations.

Methods

Participants

Participants were one hundred twenty five adults, including 63 younger adults ranging from 18 to 29 years (M=22.5, SD=2.99) and 62 older adults ranging from 60 to 75 years (M=64.5, SD=3.56). Participants were recruited from the general population. All participants completed a questionnaire related to general health and the history of psychiatric disorders including schizophrenia. None of the participants reported any current health issues. All participants were Georgian. For the genetic analysis, each participant donated 20 ml of blood. Prior to the behavioral experiment, we determined visual acuity for each participant with the Freiburg visual acuity test (FrACT, Bach 1996). One hundred and six participants (60 young/46 old) had normal or corrected-to-normal vision of 0.8 or above (M=1.39, SD=0.35). Three younger and sixteen older adults had a visual acuity below 0.8 and their data was excluded from final analysis. Hence, the final sample was composed of 106 participants. The demographic characteristics are shown in Table 1.

The study was approved by the Bioethics Committee of the Ivane Beritashvili Center of Experimental Biomedicine and was performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

Apparatus and stimuli

Stimuli were presented on a Samsung SyncMaster 957DF CRT screen with a 100-Hz refresh rate and a resolution of 1024 x 768 pixels. Stimulus luminance was 100 cd/m^2 as measured with a GretagMacbeth Eye-One Display 2 colorimeter. The background luminance of the screen was below 1 cd/m^2.

Stimuli were random dot kinematograms consisting of a field of 50 white moving dots at speed of 5.6 °/s. The dots were presented on a black background within a rectangular region (8.9x6.7 deg) in the middle of the screen and had a size of 5′. The target dots moved coherently either to the right or to the left, while the distractor dots were allocated a random direction at the beginning of each trial. Trials were separated by an interval of 500ms.

The lifetime of the dots was not limited. A dot moving out of the rectangular region reappeared at a new random position within the region and continued moving in the same direction as allocated at the beginning of the trial. A red fixation dot with a size of 8′ appeared 500ms before each trail and remained on the screen for the entire stimulus presentation (Fig.1).

Procedure

Participants were seated in a dimly lit room at 200 cm from the screen and had to indicate whether the global motion of the dots was either to the right or left by pushing a button in their right or left hand, respectively. Auditory feedback was provided. Motion coherence, i.e., the percentage of target dots, varied randomly according to a PEST procedure (Creelman and Taylor 1969). The motion coherence starting value was 20%. We determined the motion coherence threshold at 75% correct for each participant. Each participant completed 120 trials.

Genotyping

DNA was extracted from blood lymphocytes (N=125) by using a blood and tissue kit (Qiagen) according to manufacturer instructions. Forward and reverse primers 5′-CTGTCCTCCGGTATCTGTG-3′ 5′-CAGTCACTTCTGTGTCTAAG -3′ were used for amplification of relevant DNA regions by polymerase chain reaction (PCR)(Bakanidze et al. 2013). Amplification of genome fragments were carried out using Platinum PCR SuperMix reagents (Invitrogen) and GenAmp PCR System 9700 (Applied Biosystems). Primers were diluted to a 5 μM working concentration. PCR profile: 94ºC for 5 min; a touchdown of 35 cycles of 94ºC for 1 min, 56ºC for 1 min, 72ºC for 1 min, followed by a final extension at 72ºC for 7 min. An aliquot of 5 μL from each PCR was run on a 1% agarose gel to visualize the DNA fragments by SYBRSafe staining. An ExoSAP-IT cleanup reagent was used for enzymatic cleanup of amplified PCR product. Single stranded sequencing of purified amplicons was performed with the primers of PCR on ABI capillary sequencer 3130xl (Applied Biosystems) using a BigDye Terminator, version 3.1 sequencing kit. PCR fragments were sequenced in both directions to assure sequence accuracy. Analysis of the sequencing data were carried out using Geneious v10.1.3. software, the alignment of the sequences was performed with BioEdit v7.2.

Based on a previous study by Bakanidze et al. (2013), we first targeted three SNPs, namely [rs3826029] [rs2337506] [rs2337980] of CHRNA7. A single nucleotide polymorphism (SNP) [rs2337506] of the CHRNA7 was genotyped for 47 subjects out of 125 participants (25 older and 22 younger; 16 GG allele carriers, 2 AA allele carriers and 29 AG allele carriers). Since the number of AA allele carriers was very small, in a preliminary analysis, homozygotes rs2337506 GG carriers were compared with all A-allele carriers. We did not find an interaction between SNP rs2337506 with motion direction discrimination, $F(1,43)=1.27$, $p=.265$. The blood of 49 participants was genotyped for SNP rs3826029 (25 older and 24 younger; 25 CC allele carriers, 2 TT allele carriers and 22 TC allele carriers). Again, since number of TT allele

carriers was very small, we contrasted homozygotes rs3826029 CC with all T-allele carriers and did not find an interaction between SNP rs3826029 and motion direction discrimination, $F(1,45)=0.03$, $p=.863$. However, a preliminary analysis of the data from 51 participants related to SNP rs2337980 showed a significant interaction between genetic variations of SNP rs2337980 with performance of the motion direction discrimination, $F(1,47)=7.59$, $p=0.008$ (25 older and 26 younger; 23 CC allele carriers, 3 TT allele carriers and 25 TC allele carriers; CC allele carriers were contrasted with all T-allele). Based on these results, we focused our study on the SNP rs2337980.

The genotyping was carried out at the Genome Center, National Center for Disease control and Public Health, Tbilisi, Georgia. Allele frequencies were 0.59 for the C-allele and for 0.41 the T-allele. There were 43 C-allele homozygotes, 62 heterozygotes, and 20 T-allele homozygotes. The observed genotype frequencies were consistent with the Hardy-Weinberg equilibrium (X^2=0,09, P >0.05) determined by the Hardy–Weinberg equilibrium calculator (http://www.oege.org/software/hwe-mr-calc.shtml ; Rodriguez et al. 2009).

Results

We conducted an analysis of variance (ANOVA) on motion coherence thresholds with between-subject factors Genotype (CC/CT/TT) and Age group (old/young). In addition, we used bootstrapping to test the significance of the obtained effects (Efron and Tibshirani 1994). One thousand resampled data sets were used for calculating a bias-corrected and accelerated (BCa) confidence interval. We used SPSS for the statistical analyses (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp).

The 3 (Genotype) × 2 (Age Groups) ANOVA showed a main effect of Age Group $F(1, 100)=37.23$,$p<0.001$, η^2_p = .27, older adults had higher motion coherence thresholds (M= 29.64, SE=1.4) than younger adults (M= 18.14, SE= 1.26); and a main effect of Genotype $F(2, 100)=4.47$, $p=0.014$, η^2_p = .08 (Fig.2; Table 2). Post-hoc tests with Tukey's HSD confirmed

lower motion coherence thresholds for TC allele carriers compared to CC carriers p=0.057, *Cliff's* δ=.26. There were no significant differences between either the TC and TT carriers p=0.281, *Cliff's* δ=-.15,or between TT and CC carriers p=0.973, *Cliff's* δ=. 06.

Table 3 shows the mean differences between Genotype groups based on 1000 bootstrap samples. There was no interaction between Age Group and Genotype $F(2, 100)=2.06$, p= 0.133, η^2_p = .04 (Fig.2).

Discussion

We recently showed that genetic changes in the cholinergic nicotinic receptor alpha 7 subunit (CHRNA7) correlate with masking deficits in schizophrenic patients (Bakanidze et al. 2013), which we attributed to deficient neuromodulation of the cholinergic system (Herzog & Brand 2015). In particular, a single nucleotide polymorphisms of the CHRNA7 was correlated with masking performance. Here, we targeted one out of the five SNPs that were tested in the previous study on schizophrenia, namely [rs2337980] of CHRNA7, and assessed whether variations in this SNP can explain individual differences in motion direction discrimination in healthy ageing.

In accordance with previous studies, older adults had significantly higher motion coherence thresholds than younger adults (Ball & Sekuler 1986; Bennett, Sekuler & Sekuler 2007; Billino, Bremmer, & Gegenfurtner 2008; Tran, Silverman, Zimmerman & Feldon 1998; Trick & Silverman 1991). In addition, we found a strong association of the SNP rs2337980 of the CHRNA7 with motion direction discrimination. In particular, participants carrying the TC genotype performed significantly better than CC carriers, i.e., they had lower motion coherence thresholds. Surprisingly, however, we only found an overall effect of genotype but no age-related associations of motion direction discrimination, i.e., both younger and older adults were equally affected by variations in the SNP. Interestingly, previous studies have reported that CC carriers in SNP rs2337980 of the CHRNA7 perform worse in a task related to response-

inhibition (Rigbi et al, 2008), and benefit more from nicotine in task performance than TC/TT carriers (Rigbi et al, 2011). These results suggest that the CC variant in SNP rs2337980 is a disadvantageous genotype for some cognitive and perceptual functions, including motion perception.

Age-related changes in the cholinergic system affect cognition (see Dumas & Newhouse 2011) and visual processing (Ricciardi et al. 2009). However, age-related changes are unlikely to be related to variations of a single gene but rather related to complex interactions between multiple genes (Kedmi & Orr-Urtreger 2011). Therefore, further studies are needed to explore interactive effects of multiple genes within the cholinergic system to understand the involvement of the cholinergic system in motion perception with regards to healthy aging.

Based on the resource modulation hypothesis, which postulates that genetic effects on cognition are more pronounced in individuals with limited neuroanatomical or neurochemical resources (Lindenberger et al. 2008; Li et al. 2017), we expected the relationship between variations of CHRNA7 and motion perception to be more pronounced in older adults. However, despite increased motion coherence thresholds for older adults and an apparent relationship between motion coherence and genetic variations in the SNP rs2337980 of CHRNA7, we did not find a relationship between age-related decline and genetic alterations.

The absence of an interaction between age group and genotype suggests that a genetic predisposition does not contribute to the inter-individual differences in motion perception of older people, and it is possible that age-related changes are related to visual experience rather than genetic differences. Our results provide an important piece in the puzzle of understanding the underlying mechanisms of age-related changes in visual perception. However, it is important to note that we only studied two age groups and focused only on one SNP. Therefore, further studies are necessary to explore age-related associations between motion direction discrimination and genotypes across the age range, assessing other important SNPs.

In conclusion, our results support previous findings of age-related decline in motion perception. More importantly, we found a relationship between motion coherence and a genetic variation of the CHRNA7 gene, indicating a strong relationship between the nicotinic system and motion perception that is independent of age.

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References

Allen HA, Hutchinson CV, Ledgeway T, & Gayle P (2010). The role of contrast sensitivity in global motion processing deficits in the elderly. Journal of Vision 10(10):15

Aztiria E, Gotti C, Domenici L (2004). Alpha7 but not alpha4 AChR subunit expression is regulated by light in developing primary visual cortex. J Comp Neurol 480:378–391

Bach M (1996). The Freiburg visual acuity test-automatic measurement of visual acuity. Optom Vis Sci 73:49–53

Bakanidze G, Roinishvili M, Chkonia E, Kitzrow W, Richter S, Neumann K, Herzog MH, Brand A, Puls I (2013). Association of Backward Masking with Nicotine Receptor α7 Subunit Gene (CHRNA7) Polymorphism in Schizophrenia. Front Psychiatry 22;4:133

Ball K, Sekuler R (1986). Improving visual perception in older observers. Journal of Gerontology 41(2): 176–182

Bennett PJ, Sekuler R, Sekuler AB (2007). The effects of aging on motion detection and direction identification. Vision Research 47(6):799–809

Billino J, Bremmer F, Gegenfurtner KR (2008). Differential aging of motion processing mechanisms: evidence against general perceptual decline. Vision Research 48(10): 1254–1261

Billino J, Hamburger K, Gegenfurtner KR (2009). Age effects on the perception of motion illusions. Perception 38(4):508–521

Billino J, & Pilz KS (2019). Motion perception as a model for perceptual ageing. Journal of vision 19(4). https://doi.org/10.1167/19.4.3

Chen Y, Nakayama K, Levy D, Matthysse S, Holzman P (2003). Processing of global, but not local, motion direction is deficient in schizophrenia. Schizophrenia Research 61(2-3): 215–227

Creelman CD, Taylor MM (1969). Some pitfalls in adaptive testing: comments on "temporal integration and periodicity pitch." Journal of the Acoustical Society of America 46: 1581–1582

Dai D, Wang Y, Yuan J, Zhou X, Jiang D, Li J, Zhang Y, Yin H, Duan S (2014). Meta-analyses of 10 polymorphisms associated with the risk of schizophrenia. Biomed Rep 2:729-736

De Leon J, Diaz FJ (2005). Ameta-analysis of worldwide studies demonstrates an association between schizophrenia and tobacco smoking behaviors. Schizophr. Res 76 (2-3):135–157

Deutsch SI, Urbano MR, Burket JA, Herndon AL, Winebarger EE (2011). Pharmacotherapeutic implications of the association between genomic instability at chromosome 15q13.3 and autism spectrum disorders. Clin Neuropharmacol, 34,203–205

Disney AA, Aoki C, Hawken MJ (2007). Gain modulation by nicotine in macaque v1.Neuron 56:701-13

Dumas JA, Newhouse PA (2011). The Cholinergic Hypothesis of Cognitive Aging Revisited Again: Cholinergic Functional Compensation. Pharmacol Biochem Behav 99(2): 254–261

Chen Y, Nakayama K, Levy D., Matthysse S, Holzman P (2003) Processing of global, but not local, motion direction is deficient in schizophrenia. Schizophrenia Research 61(2-3): 215–227

Efron B, Tibshirani RJ (1994). An introduction to the bootstrap. CRC press

Fernandez R, Monacelli A, Duffy CJ (2013) Visual motion event related potentials distinguish aging and Alzheimer's disease. J Alzheimers Dis 36(1):177-83

Galvin VC, Amsten AFT, Wang M (2018). Evolution in neuromodulation – the differential roles of acetylcholine in higher order association vs. primary visual cortices.

Gotti C, Moretti M, Gaimarri A, Zanardi A, Clementi F, Zoli M (2007). Heterogeneity and complexity of native brain nicotinic receptors. Biochem Pharmacol 74:1102–1111

Herzog MH, Brand A (2015) Visual masking & schizophrenia. Schizophrenia Research: Cognition 2:64-71

Hutchinson CV, Arena A, Allen HA, Ledgeway T (2012). Psychophysical correlates of global motion processing in the aging visual system: a critical review. Neurosci Biobehav Rev

36:1266-72

Hutchinson CV, Ledgeway T, Allen HA. (2014). The ups and downs of global motion perception: a paradoxical advantage for smaller stimuli in the aging visual system. Front Aging Neurosci. doi: 10.3389/fnagi.2014.00199. eCollection 2014

Kang JI, Huppé-Gourgues F, Vaucher F (2014) Boosting visual cortex function and plasticity with acetylcholine to enhance visual perception. Front Syst Neurosci. doi:10.3389/fnsys.2014.00172

Kedmi M, Orr-Urtreger A (2011). The effects of aging vs. α7 nAChR subunit deficiency on the mouse brain transcriptome: aging beats the deficiency. Age (Dordr) 33:1-13

Koldewyn K, Whitney D, Rivera SM (2010). The psychophysics of visual motion and global form processing in autism. Brain: A Journal of Neurology 133:599–610

Kunchulia M, Pilz KS, Herzog MH (2014). Small effect of Nicotine of visual spatiotempotal processing. Scientific Reports 4,7316

Leonard S, Mexal S, Freedman R (2007). Smoking, genetics and schizophrenia: evidence for self-medication. J. Dual Diagn 3: 43–59

Li X, Papenberg G, Kalpouzos G, Вдckman L, Persson J (2017). Influence of the DRD2/ANKK1 Taq1A polymorphism on caudate volume in older adults without dementia. Brain Structure and Function. doi.org/10.1007/s00429-018-1650-0

Lindenberger U, Nagel IE, Chicherio C, Li SC, Heekeren HR, Bäckman L (2008). Age-related decline in brain resources modulates genetic effects on cognitive functioning. Front. Neurosci 2:234–244

McCool C. H. Britten K. H. (2008). Cortical processing of visual motion. In Basbaum A. I. Kaneko A. Shepherd G. M. Westheimer G. Albright T. D. Masland R. H. Dallos P. Oertel D. Firestein S. Beauchamp G. K. Bushnell M. C. Kaas J. H. Gardner E. (Eds.), *The senses: A comprehensive reference* (pp. 157–187). New York: Academic Press.

Maunsell JH, Nealey TA, & DePriest DD (1990). Magnocellular and parvocellular contributions to responses in the middle temporal visual area (MT) of the macaque monkey. Journal of Neuroscience 10: 3323–3334

Norman JF, Cheeseman JR, Pyles J, Baxter MW, Thomason KE, Calloway AB (2013). The effect of age upon the perception of 3-D shape from motion. Vision Research 18:54-61

Origlia N, Valenzano DR, Moretti M, Gotti C, Domenici L (2012). Visual acuity is reduced in alpha 7 nicotinic receptor knockout mice. Invest Ophthalmol Vis Sci 53:1211-8

Peng ZZ,Wan XN, Jiang TY, Cheng L, Sun BL, Hong XH (2007). Association between neuronal nicotinic acetylcholine receptor α7 subunit gene polymorphism and schizophrenia. Journal of Shantou University Medical College 20:213–219

Papenberg G, Lindenberger U, Bäckman L (2015). Aging-related magnification of genetic effects on cognitive and brain integrity. Trends Cogn Sci 19:506-14

Papenberg G, Salami A, Persson J, Lindenberger U, Bäckman L (2015). Genetics and Functional Imaging: Effects of APOE, BDNF, COMT, and KIBRA in Aging. Neuropsychol Rev 25:47–62

Parri HR, Hernandez CM, Dineley KT (2011). Research update: Alpha7 nicotinic acetylcholine receptor mechanisms in Alzheimer's disease. Biochem Pharmacol 82(8):931–942

Pilz KS, Miller L, Agnew HC (2017). Motion coherence and direction discrimination in healthy aging. Journal of Vision (1),31. doi: 10.1167/17.1.31

Pilz KS, Kunchulia M, Parkosadze K, Herzog MH (2015). Ageing and visual spatiotemporal processing. Experimental Brain Research 233(8): 2441–2448

Rigbi A, Kanyas K, Yakir A, Greenbaum L, Pollak Y, Ben-Asher E, Lancet D, Kertzman S, Lerer B (2008). Why do young women smoke? V. Role of direct and interactive effects of nicotinic cholinergic receptor gene variation on neurocognitive function. Genes Brain Behav 7(2):164-72

Rigbi A, Yakir A, Sarner-Kanyas K, Pollak Y, Lerer B (2011). Why do young women smoke? VI. A controlled study of nicotine effects on attention: pharmacogenetic interactions. Pharmacogenomics Journal 11(1):45-52

Ricciardi E, Pietrini P, Schapiro MB, Rapoport SI, Furey, M (2009). Cholinergic modulation of visual working memory during aging: a parametric PET study. Brain Res Bull 79(5):322-32

Rodriguez S, Gaunt T, Day I (2009). Hardy-Weinberg Equilibrium Testing of Biological Ascertainment for Mendelian Randomization Studies. Am J Epidemiol 169:505–514

Rokem A, Silver MA (2010). Cholinergic enhancement augments magnitude and specificity of visual perceptual learning in healthy humans. Curr. Biol 20:1723–1728. 10.1016/j.cub.2010.08.027

Severance EG, Yolken RH (2008). Novel alpha7 nicotinic receptor isoforms and deficient cholinergic transcription in schizophrenia. Genes Brain Behav 7(1):37–45

Shain LM, Norman JF (2018). Aging and the Visual Perception of Motion Direction: Solving the Aperture Problem. Perception 47(7):735-750

Shaqiri A, Clarke A, Kunchulia M, Herzig D, Pilz KS, Herzog MH (2015). The effects of aging on perception and cognition. Journal of Vision 15(12): 802. doi:10.1167/15.12.802

Snowden R, Kavanagh E (2006). Motion perception in the ageing visual system: minimum motion, motion coherence, and speed discrimination thresholds. Perception 35(1):9-24

Spencer JM, Sekuler AB, Bennett PJ, & Christensen BK (2013). Contribution of coherent motion to the perception of biological motion among persons with Schizophrenia. Frontiers in Psychology 4, 507, doi:10.3389/fpsyg.2013.00507.

Tran DB, Silverman SE, Zimmerman K, Feldon SE (1998). Age-related deterioration of motion perception and detection. Graefe's Archive for Clinical and Experimental Ophthalmology 236(4):269–273

Trick GL, Silverman SE (1991). Visual sensitivity to motion: Age-related changes and deficits in senile dementia of the Alzheimer type. Neurology 41(9): 1437–1440

Table 1. Demographic characteristics of groups genotyped for a single nucleotide polymorphism (SNP) [rs2337980] of the CHRNA7

Genotype	N	Age Old/Young	Sex F/M
CC	40	M=38.93 SD=21.24 15/25	22/18
TC	49	M=41.63 SD=21.83 23/26	28/21
TT	17	M=42 SD=20.9 8/9	9/8

Table 2. Estimated Marginal Means of motion coherence thresholds for the Genotype Groups with BCa 95% confidence interval based on 1000 bootstrap samples.

Genotype	Mean	95%CI range on based 1000 bootstrap samples
CC	M=26.201 SE=1.417	23.215- 29.095
TC	M=20.726	18.342- 22.929

	SE=1.242	
TT	24.74 SE=2.242	20.375- 28.835

Table 3. Mean differences in motion coherence thresholds between Genotype groups based on 1000 bootstrap samples.

Genotype	Mean differences	95%CI range on based 1000 bootstrap samples
CC-TC	4.3	.44-8.57
CC-TT	.56	-5.06- 6.47
TT-TC	3.73	-2.64- 10.41

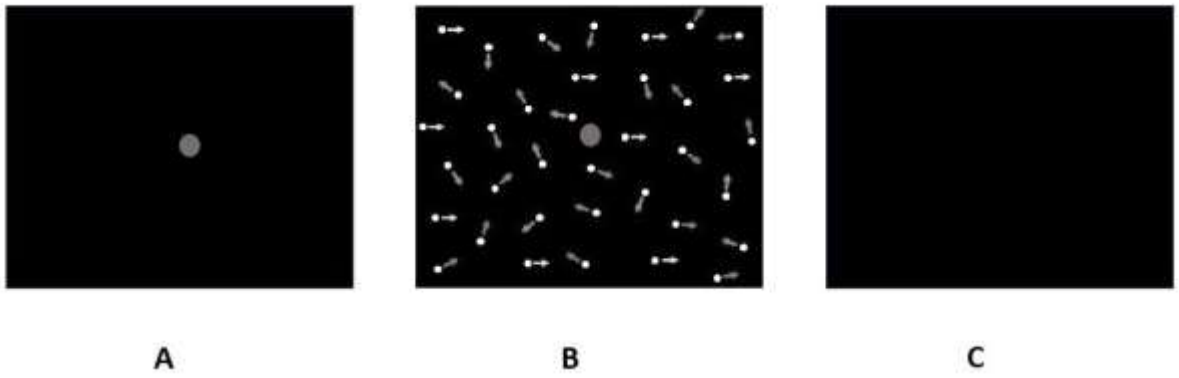

Figure 1. Example of a trial structure. Each trial began with a presentation of the red fixation dot (A). B) Shows white dots stimuli. Target dots moved coherently to the right or to the left, while distractor dots moved randomly. Central red fixation dot was maintained during stimuli presentation. The trials were separated by inter-trial interval (ITI) of 500 ms (C). Participants had to indicate left or right moving direction of target dots.

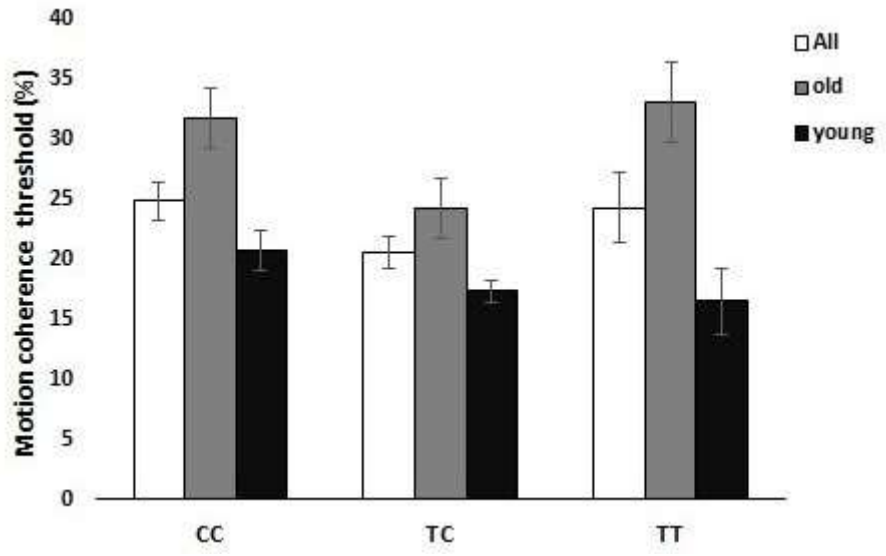

Figure 2. Mean motion coherence thresholds for CC, TT, TC carriers for all participants, for older and younger participants. The thresholds are plotted as the percentage of target dots. Errors bars show standard errors of the mean. Participants carrying the TC genotype performed the task significantly better than CC carriers. Older adults had higher motion coherence thresholds than younger ones.