Psychiatry Research: Neuroimaging 256 (2016) 8–14

Contents lists available at ScienceDirect

Psychiatry Research: Neuroimaging

journal homepage: www.elsevier.com/locate/psychresns

Associations between corpus callosum size and ADHD symptoms in older adults: The PATH through life study

Eileen Luders [a,b], Florian Kurth [a], Debjani Das [c], Daniela E. Oyarce [b], Marnie E. Shaw [b], Perminder Sachdev [d], Simon Easteal [c], Kaarin J. Anstey [b], Nicolas Cherbuin [b,*]

[a] Cousins Center for Psychoneuroimmunology, Semel Institute for Neuroscience and Human Behavior, Department of Psychiatry and Biobehavioral Sciences, UCLA School of Medicine, Los Angeles, USA
[b] Centre for Research on Ageing Health and Wellbeing, Australian National University, Canberra, Australia
[c] John Curtin School of Medical Research, Australian National University, Canberra, Australia
[d] School of Psychiatry, University of New South Wales, Sydney, Australia

ARTICLE INFO

Article history:
Received 12 January 2016
Received in revised form
22 May 2016
Accepted 25 August 2016
Available online 26 August 2016

Keywords:
Aging
Brain
Hyperactivity
Inattention
MRI
Sexual dimorphism

ABSTRACT

Neuroimaging studies of attention-deficit/hyperactivity disorder (ADHD) have revealed deviations of the corpus callosum in children and adolescents. However, little is known about the link between callosal morphology and symptoms of inattention or hyperactivity in adulthood, especially later in life. Here, we investigated in a large population-based sample of 280 adults (150 males, 130 females) in their late sixties and early seventies whether ADHD symptoms correlate with callosal thickness. In addition, we tested for significant sex interactions, which were followed by correlation analyses stratified by sex. Within males, there were significant negative correlations with respect to inattention and hyperactivity in various callosal regions, including the anterior third, anterior and posterior midbody, isthmus, and splenium. A thinner corpus callosum may be associated with fewer fibers or less myelination of fibers. Thus, the observed negative correlations suggest impaired inter-hemispheric communication channels necessary to sustain motor control and attention, which may contribute to symptoms of hyperactivity, impulsivity and/or inattention. Interestingly, within females, callosal thickness was positively related to hyperactivity in a small area within the rostral body, suggesting a sexually dimorphic neurobiology of ADHD symptoms. Altogether, the present results may reflect a lasting relationship between callosal morphology and ADHD symptoms throughout life.

1. Introduction

Converging evidence suggests a neurobiological basis for attention-deficit/hyperactivity disorder (ADHD). While its precise etiology remains unclear, one of the most replicated structural alterations in ADHD is a significantly smaller corpus callosum (Seidman et al., 2005). Meta-analytic findings suggest the callosal splenium (Valera et al., 2007) as well as the forceps minor (van Ewijk et al., 2012) to be particularly affected. However, ADHD-related callosal abnormalities have also been reported for the isthmus (Lyoo et al., 1996), the anterior midbody (Cao et al., 2010), the rostral body (Baumgardner et al., 1996; Giedd et al., 1994), the genu (Hynd et al., 1991), the rostrum (Giedd et al., 1994), as well as the corpus callosum as a whole (Hill et al., 2003). The aforementioned callosal subsections (with exception of the forceps minor, a fiber bundle crossing through the genu) refer to the well-established Witelson scheme (Witelson, 1989), as illustrated in Fig. 1.

In contrast to an abundance of ADHD studies and callosal findings in children and adolescents (i.e., all of the studies mentioned above were conducted in pediatric samples), little is known about links between callosal morphology and symptoms of inattention or hyperactivity in adulthood. The sparseness of findings with respect to adult ADHD-related variations in callosal morphology (or brain features in general) may be largely due to the fact that ADHD, as we know it today, has only been defined relatively recently (Lange et al., 2010). More specifically, the first characterization of the disorder was added to the DSM-II in 1968, but the actual name was only implemented as “attention deficit disorder: with and without hyperactivity” in 1980 (DSM-III), followed by “attention deficit hyperactivity disorder” in 1987 (DSM-III-R). Still, a few adult studies exist and point to ADHD-related callosal abnormalities later in life: For example, Dramsdahl and colleagues examined 29 individuals with ADHD and 37 controls (mean age of 32.9 years) complementing MRI- and DTI-based measures in a region-of-interest analysis focusing on the corpus

* Corresponding author.
E-mail address: nicolas.cherbuin@anu.edu.au (N. Cherbuin).

http://dx.doi.org/10.1016/j.pscychresns.2016.08.009
0925-4927/

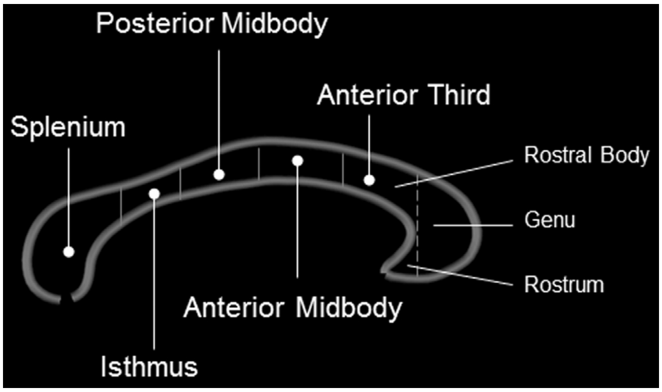

Fig. 1. Callosal subsections. Visualized are callosal segments according to the Witelson parcellation scheme (Witelson, 1989). The posterior end of the corpus callosum points to the left; the anterior end points to the right.

callosum. Specifically, they compared fractional anisotropy (a measure of diffusion directional anisotropy) as well as the size of callosal subdivisions between the two groups. The study revealed a significantly reduced fractional anisotropy within the ADHD group for the isthmus/splenium but no group differences with respect to the size of the callosal subdivisions (Dramsdahl et al., 2012). A couple of years later, Chaim and colleagues examined 22 individuals with ADHD and 19 controls (mean age of 28.8 years and 28.7 years, respectively) using MRI- and DTI-based measures and applying optimally-discriminative voxel-based (ODVB) analyses. Specifically, they compared fractional anisotropy as well as trace (a measure of diffusivity) between the two groups. With respect to the corpus callosum (there were significant effects in other brain regions as well), the study revealed reductions in trace in the ADHD group within the callosal body and splenium (Chaim et al., 2014). Finally, Onnink and colleagues examined 107 individuals with ADHD and 109 controls (mean age of 35.0 years and 36.1 years, respectively) using DTI-based measures and applying tract-based spatial statistics (TBSS). Specifically, they compared fractional anisotropy as well as mean, axial, and radial diffusivity between the two groups. With respect to the corpus callosum (there were also significant effects in other brain regions), the study revealed a significantly lower fractional anisotropy in the ADHD group within the callosal body and splenium as well as a significantly higher mean and radial diffusivity within the callosal body, splenium, and genu (Onnink et al., 2015).

To further expand this understudied field of research, the current MRI-based study was designed to establish the presence and direction of possible links between ADHD symptoms and callosal morphology later in life. For this purpose, we administered the ADHD Self-Report Scale (ASRS), which was developed by the World Health Organization to enable assessment of ADHD symptoms without the necessity of a diagnosis. The ASRS was not only found to have good validity in younger samples with an ADHD diagnosis (Sonnby et al., 2015) but also demonstrated in older cohorts significant links between ADHD symptoms and daily functioning as well as mental health, cognition, and brain anatomy (Das et al., 2012, 2014a, 2014b). Here, we investigated a large sample of 280 adults (mean age of 70.93 years) and applied a well-validated computational approach capturing the thickness of the corpus callosum at 100 equidistant locations across the callosal surface. We hypothesized ADHD symptoms would be negatively associated with callosal thickness. We also tested for significant sex interactions and conducted follow-up analyses stratified by sex (150 males, 130 females) as both the prevalence and the presentation of ADHD appear to differ between the sexes (Davies, 2014). Last but not least, we investigated whether the significant associations between ADHD symptomatology and callosal thickness in this adult sample would resemble those revealed when contrasting children with ADHD (mean age of 11.7 years) and their age-matched controls in a previous study using the same callosal approach (Luders et al., 2009). Specifically, we had detected that ADHD was associated with a decreased callosal thickness in regions corresponding to the anterior third (mainly genu and rostral body), isthmus, and splenium (mainly anterior splenial section).

2. Methods

2.1. Subjects

The study sample was drawn from the PATH through life project, a large longitudinal study of mental health and aging, as detailed elsewhere (Anstey et al., 2012). The study was approved by the ethics committees of the Australian National University, Canberra and the University of New South Wales, Sydney, Australia. All participants gave written informed consent to be included in this project. The present study focuses on the old-age cohort, which included 2551 individuals aged 60–64 years at the start of the project. A subsample of 2076 agreed to be contacted regarding MRI assessment, 622 randomly selected participants were offered a brain scan, and 479 completed a structural MRI scan at first assessment (Wen et al., 2009). Of those, 315 participants had a repeat structural MRI scan at the third assessment (wave three), which is the focus of this study (as the ASRS was first administered at wave three). After excluding 35 MRI scans due to movement artifacts, poor scan quality, truncation, neurological disorders and participants who did not complete the ASRS questionnaire, the final sample of the current study consisted of 280 subjects (150 males, 130 females) ranging from 68.6 to 73.8 years of age. This selected sample ($n=280$) did not differ from the original cohort ($n=2551$) or from those only surveyed (but not scanned) at the third assessment ($n=1973$) in age, sex, or race. However, they had on average a slightly (about seven months at first assessment and four months at third assessment) but significantly ($p<0.05$) higher level of education.

2.2. ADHD measures

ADHD-related measures were obtained using the ASRS, a checklist of six questions regarding symptoms of ADHD based on the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) (Hesse, 2013; Kessler et al., 2005; Kessler et al., 2007). Each item requires respondents to rate how frequently a particular symptom of ADHD occurred over the past six months on a 5-point scale (from 0=never to 4=very often). A summary score (ASRS) with a possible range of 0-24 was obtained as an equally weighted sum of response scores for all questions, with higher scores indicating increased risk of ADHD. As previously described (Das et al., 2012), the first four items of the ASRS screener capture inattention-related symptoms, while the remaining two items assess hyperactivity-related symptoms. Thus, in addition to the overall ASRS score, we also calculated an Inattention Trait (IT) score using the equally weighted sum of the first four items, as well as a Hyperactivity Trait (HT) score using the equally weighted sum of the last two items.

2.3. Image acquisition and data preprocessing

All brain images were acquired on a Siemens 1.5 T Avanto scanner (Siemens Medical Solutions) in sagittal orientation using the following scanning parameters: TR=1160 ms, TE=4.17 ms, flip angle=15°, matrix size=512 × 512, slice thickness=1 mm, voxel