investigating iPSCs and NPCs without treatment showed overall no significant differences in total protein expression between ADHD (n=7) and control (n=12) groups (Mann Whitney, n.s.). However, in NPCs a tendency in decreased LRP6 protein could be observed, while β -Catenin and GSK3β remain similar in total protein expression between ADHD to control. However, considering GSK3β phosphorylation ratios we could observe a decrease in ADHD (Mann Whitney, *p=0.0275). xCELLigence results of NPCs without treatment showed a significant decrease in ADHD compared to control (Mann Whitney, ***p=0.0001).

Conclusion: Our results indicate proteomic changes throughout different cell developmental stages with minor differences in ADHD. More importantly GSK3β phosphorylation ratios indicating differences in activity, may be due to compensations towards altered Wnt activity. However, further analysis is relevant to validate these assumptions. Alas, our findings will contribute to understanding the importance of the Wnt pathway more evidently and furthermore may reveal the functional effects ω-3 PUFA in Wnt-signalling and development, to be considered as an alternative treatment approach in ADHD.

No conflict of interest

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Development of a human-based, disease-relevant in vitro model to investigate the ADHD risk gene ADGRL3 in disease aetiology

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Background and Aims: Attention-deficit/hyperactivity disorder (ADHD) is a complex, chronic neuropsychiatric disorder, which significantly impairs life quality and is associated with premature death. Typical symptoms include inattention, hyperactivity, and emotional/motivational dysregulation. Although both dopaminergic and glutamatergic pathways are thought to play a role in the disorder, its exact aetiology remains poorly understood. Further hindering understanding is a lack of suitable in vitro models. Single nucleotide polymorphisms (SNPs) in the adhesion G protein-coupled receptor L3 (ADGRL3/LPHN3) gene have been robustly associated with ADHD, and deletion of ADGRL3 in animal models has been reported to cause ADHD-like symptoms. The receptor is thought to play a role in glutamatergic synapse development, synaptic plasticity, and calcium signalling. However, the potential function of this receptor in disease pathogenesis is unclear. We therefore aimed to develop a human-based, disease-relevant in vitro model for the investigation of ADGRL3 in ADHD pathogenesis, using human induced pluripotent stem cells (hiPSCs) differentiated into cortical neurons.

Methods: Quality-controlled hiPSCs were generated from three healthy controls and three ADHD patients carrying different genotypes for the ADGRL3 ADHD risk SNP rs1397547. One clone from each cell line was differentiated into neural progenitor cells (NPCs) using a small molecule-based method. NPCs were further differentiated into cortical neuron cultures for 8 weeks using a neurobasal media supplemented with cyclic AMP and ascorbic acid. RNA and protein were extracted for RT-qPCR and western blotting to determine ADGRL3 expression. Cells were also fixed for immunofluorescence (IF) analysis to determine the identity of resultant cultures, and calcium imaging was performed to assess spontaneous signalling.

Results: NPCs were successfully generated from all donors, as confirmed by IF labelling of the NPC markers PAX6 and SOX2. PAX6 expression additionally suggested that the NPCs were of a forebrain identity. IF analysis of 8-week-old cortical neurons revealed that the majority of cells expressed TUBB3, indicating a neuronal identity. Moreover, most TUBB3+ cells also demonstrated vGLUT2 expression, suggesting that neurons were predominantly glutamatergic. The expression of pre- and post-glutamatergic synapse proteins further demonstrated the development glutamatergic synapses. Astrocytes were also identified within the cultures, an important tenet for neurotransmission. Calcium imaging confirmed spontaneous signalling events within the cultures, suggesting the presence functionally mature neurons capable of firing action potentials. Lastly, ADGRL3 transcript and protein was found expressed in the cortical neuron cultures. ADGRL3 protein appeared predominantly localised to axons and dendrites, consistent with its role in glutamatergic synapse development and axon guidance.

Conclusions: We were able to generate hiPSC-derived functionally mature cortical neuron cultures from both healthy controls and ADHD patients. Moreover, we confirmed expression of the ADHD risk gene ADGRL3 in our model. This research provides a novel tool for the investigation of ADHD pathogenesis and potential drug screening in a human-based, disease-relevant model. Future work aims to determine the possible effects of ADGRL3 SNPs on its expression and glutamatergic neuron development, and extensive characterisation of the model, for example via single cell-RNA sequencing.

No conflict of interest

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The acceptability of remote measurement technology in the long-term monitoring of individuals with ADHD – a qualitative analysis

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Introduction: Remote measurement technology (RMT) allows continuous collection of real-time data for longer periods. RMT incorporates active (e.g. questionnaires) and passive (e.g. smartphone sensors and wearable devices) monitoring. Building on the 'RADAR-base' mobile-health platform [1], we have recently developed a set of remote measures for adolescents and adults with attention deficit hyperactivity disorder (ADHD): the ADHD Remote Technology ('ART') system. The ART pilot study involved a 10-week study period using RMT. Debrief interviews were completed to provide novel perspectives of the acceptability and feasibility of RMT in individuals with ADHD and controls.

Previous research has focused on exploring anecdotal views and attitudes towards digital technology in individuals with ADHD [2]; however, to our knowledge, there is no previous research that has used qualitative methods to understand the end-point acceptability of RMT in participants with ADHD. The addition of a control group is also a novel approach in qualitative feedback on RMT. The aim of this study is to evaluate the acceptability of RMT in both individuals with ADHD and a control group. We were also interested in participants' views on using RMT in future studies with longer duration.

Methods: Twenty adults and adolescents with ADHD and twenty control participants were followed-up for 10 weeks using RMT that involved (questionnaires, cognitive tasks) and passive (smartphone, wearable device) monitoring. Semi-structured qualitative interviews were completed at the end of the study period. ADHD diagnosis was confirmed by the Diagnostic Interview for ADHD in adults at baseline. Participants were not taking medication for ADHD. Individuals with ADHD (M=27.49, SD=6.04) and controls (M=27.79, SD=6.17) did not differ on age ($p>0.05$) or sex ($p>0.05$).

Ten adults with ADHD and twelve controls completed the interviews at the end of the study period. Although the sample size is smaller than the whole sample, debrief interviews were completed once the interviews reached saturation [3]. All interviews were audio-recorded and transcribed verbatim. All transcripts were coded by two researchers working independently. The coding frame was built on barriers and facilitators to engagement with RMT identified by Simblett and colleagues [4].

Summary of Results: Four key themes emerged across the two groups. Participants noted the health-related (theme 1) benefits of taking part in the study, including insight and improvements to their sleep, physical activity, lifestyle and mood. In terms of user-related (theme 2) experience with the questionnaires, smartphone and wearable device in the ART system, feedback was positive, with participants describing the study as enjoyable and interesting and that the study blended into their daily life. When it came to more technology-related (theme 3) outcomes, participants described the passive data as objective and felt it was more accurate than manually recording it, but some described difficulties with