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Letter to the Editor

Motor sequence learning and pattern recognition in youth at clinical high-risk for psychosis

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Dear Editors,

Implicit motor sequence learning (MSL), a foundational cognitive process that reflects the confluence of basic learning and motor function, is impaired in psychotic disorders such as schizophrenia (Chrobak et al., 2017; Clark and Lum, 2017; Green et al., 1997). Implicit MSL task, like the serial response task (SRT; Howard et al., 2004), can distinguish deficits due to dopaminergic effects from issues related to explicit cognitive deficits (which occur in pattern recognition, see Song et al., 2009) or hippocampal-dependent MSL deficits (which occur in earlier trials, see Gamble et al., 2014). As a result the SRT is ideal for studying mechanisms and identifying markers in the clinical high-risk (CHR) period, where abnormalities in cerebellar, hippocampal, and striatal/dopaminergic systems are implicated in emerging psychosis (Mittal et al., 2017). However, despite this promising convergence, to date, there have been no studies examining MSL in CHR individuals. To address this gap in the literature, the present study examines CHR performance on the SRT in terms of median reaction time, accuracy, and the recognition of the pattern across blocks and sequences. We expect that CHR individuals will show similar deficits in the rate of MSL as previously observed in psychosis (Chrobak et al., 2017; Clark and Lum, 2017; Green et al., 1997), while they may appear intact in block-level metrics of learning (Green et al., 1997; Purdon et al., 2011; Woodward et al., 2007).

Participants (35 CHR, 22 Control) between the ages of 15 and 24 were recruited for this study. CHR group was defined by the presence of a prodromal syndrome, as measured by the Structured Interview for Prodromal Syndromes (SIPS; McGlashan et al., 2001). Exclusionary criteria included the presence of an Axis I past or current psychotic disorder, which was assessed with the Structured Clinical Interview for Axis-I DSM-IV Disorders. The Institutional Review Board approved the protocol and informed consent procedures, and all participants provided informed consent. The serial response task (SRT) indexed implicit MSL using metrics calculated from repeating sequences (Fig. 1A). The task consisted of 6 blocks of 50 trials (either random or repeated blocks). Random blocks had trials in a pseudorandomized order such that strings of trials would not be repeated. Repeated sequence blocks had five repetitions of 10-trial sequences. At the end of each block, participants were prompted to rate whether there was pattern on a four-point scale (pattern recognition; see Fig. 1C), which was followed by a 5 s break between the blocks. Reaction time and accuracy were recorded in *E*-Prime 2.0 for all responses (Psychology Software Tools, Inc., 2002). All analyses were restricted to repeated blocks (Chrobak et al., 2017; Howard et al., 2004), and reaction times analysis is restricted to correct responses. Median reaction times were calculated for each 10-item sequence to ensure that reaction times were not biased toward any single slow response as in previous literature (Chrobak et al., 2017; Green et al., 1997; Howard et al., 2004; Purdon et al., 2011; Woodward et al., 2007). Accuracy was also calculated for each 10-item sequence, resulting in one accuracy score for each repetition of a sequence. Finally, pattern recognition responses were treated as binary (e.g., yes for maybe and definitely responses) to calculate accuracy.

Separate repeated measures ANOVA examined median reaction time and accuracy of first response for sequences (5 repetitions) nested in blocks (3 repeated sequence blocks) which were compared across groups (CHR and HC). There were no significant main or interactive effects of group on mean of median reaction times, $p's > .47$. There was a significant group by sequence interaction, $F(4,440) = 3.20$, $p = .01$. Post-hoc analyses revealed that this interaction was driven by the fourth repetition, $p = .02$, (Fig. 1B). There were no other significant main or interactive effects of group, $p's > .33$. Finally, a repeated measure ANOVA examined accuracy of pattern recognition by block (3 repeated sequence blocks) which were compared across groups (CHR and HC). There was a significant group by block interaction, $F(2,112) = 3.14$, $p = .04$. Post-hoc analyses revealed that this interaction was driven by the second block, $p = .02$, and a significantly different curvilinear interaction where CHR show a u-shaped curve of increased recognition and HC show an inverted-u shaped curve, $F(1,56) = 5.33$, $p = .03$, Fig. 1C. There were no other significant main or interactive effects of group, $p's > .20$.

We observed that while CHR individuals show similar model-level MSL when compared with controls, both the learning rate and pattern recognition accuracy are impacted in this group. This pattern (no group differences at the model-level but specific rate-level deficits) is broadly consistent with what has been observed in chronically psychotic groups (Green et al., 1997). These results are also consistent with research in first-degree relatives (Woodward et al., 2007) and first-episode psychosis (Purdon et al., 2011), which found no group differences on block-level MSL though rate of learning and pattern accuracy were not evaluated in these studies. Although we do not have data at this level, a broader SRT literature suggests the timing of this group difference suggests that CHR individuals show intact in early hippocampal-dependent learning processes, but may have deficits in dopaminergic-dependent learning (Gamble et al., 2014). One possibility is that hippocampal dependent-learning is impacted later in the development of psychosis whereas dopaminergic-dependent learning may reflect early emerging signs (Howes et al., 2009). Finally, pattern recognition analyses revealed a significant group by block interaction, in which CHR individuals showed a u-shaped recognition of pattern compared to the HCs inverted u-shaped pattern recognition. This finding may indicate disruption in the transitions between explicit and implicit MSL systems (Song et al., 2009).

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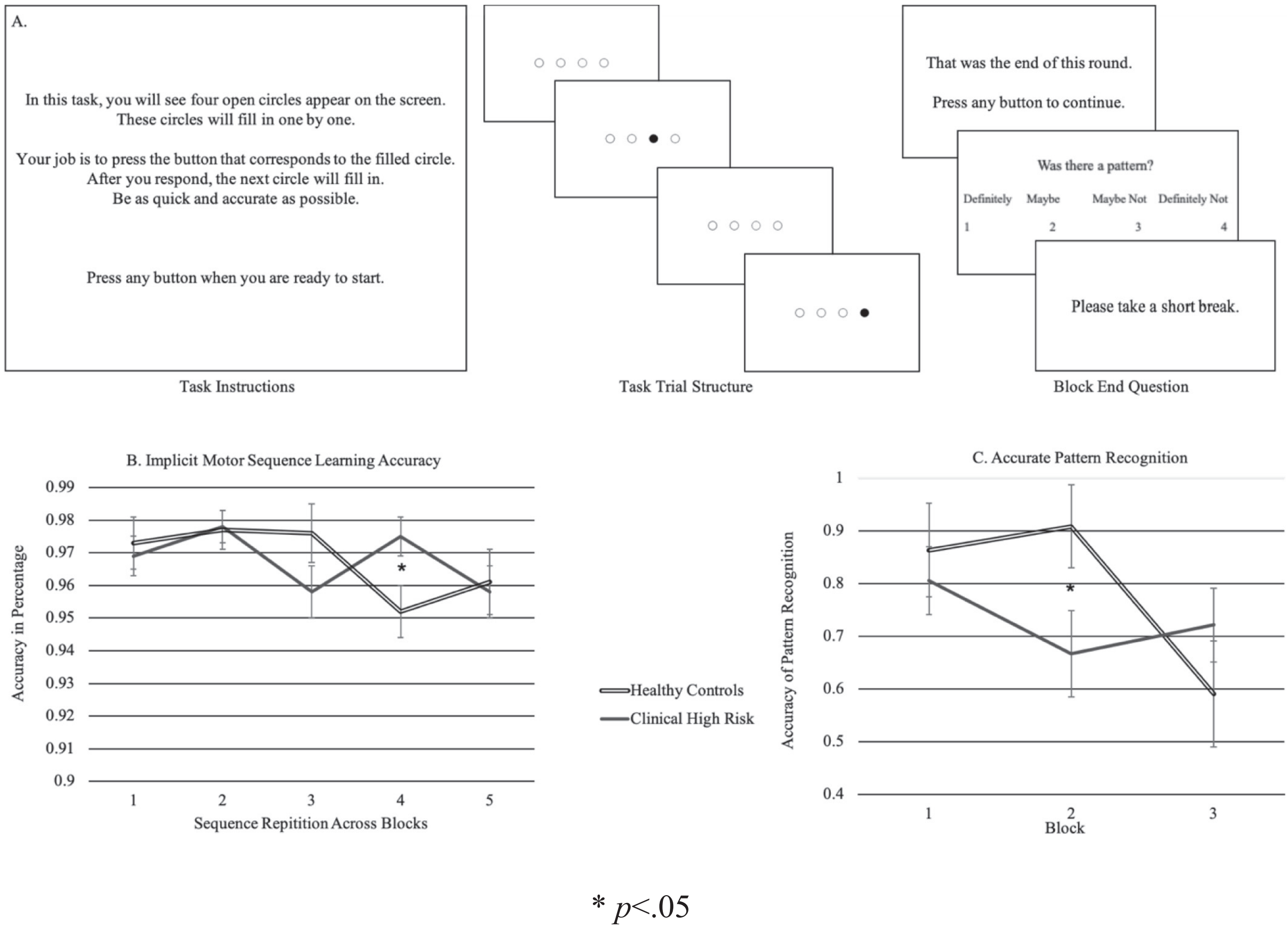

Fig. 1. Serial response task paradigm (A); group differences in implicit motor sequence learning accuracy (B) and pattern recognition accuracy (C).

Future studies should further investigate whether these group differences reflect disruptions in transitions between transition to dopamine-dependent learning (Gamble et al., 2014) or in the interplay between implicit and explicit pattern recognition (Song et al., 2009). If present, these network transition deficits may be a target for treatment.

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Conflicts of interest

We have no conflicts to disclose.

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